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British Journal of Anaesthesia

JOINT EDITORS:

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Editor of Postgraduate Educational Numbers R. P. HARBORD

JUL 7 1959

University of Kansas
Medical Center

Volume XXXI No. 5 May 1959

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BRITISH JOURNAL OF ANAESTHESIA

VOL. XXXI, No. 5 MAY 1959

EDITORIAL

HOLIDAYS

THE Summer is upon us and it may not be too frivolous to give some thought in these columns to the question of holidays—in N.H.S. parlance "annual leave". It is the impression of the writer that men of the older generation of practitioners considered a holiday to be a necessary and useful prescription for their patients, but quite unnecessary and even a little infra dig. for themselves or their colleagues. To plan them with anticipation was regarded as evidence of a flippant and irresponsible nature and of a man not really having his mind on his true vocation. It was not uncommon for men to go many years without a reasonable break in the daily round and hospital practice. Humphrey Rolleston (1925) told us that Sir James Paget did without a holiday for fifteen years during his hard struggle as a young "surgeon-pathologist". Self-indulgence of this nature would seem to us of the present coronary-prone generation likely to result in a long journey which in no sense could be regarded as a holiday.

It is common experience that the urge to take holidays plotted against years of age follows a U-shaped curve, being considerable in youth, slightly less in early manhood, decreasing with the onset of career-ambition and financial responsibilities, and reaching a nadir, perhaps, in early middle age, when the increasing exigencies and irritant stresses of family holidays combined with a subconscious fear of a declining practice at home make them almost purgatorial. At this stage a man not infrequently must exercise sufficient self-denial to force himself to take them—almost like the proverbial unpleasant and bitter bottle of tonic. With advancing years, however, accompanied by secure success or resigned failure, the urge to break away may return.

Our "State" with parental (or is it maternal?) solicitude allows each consultant 6 weeks out of the 52 for holidays—but how many in fact do or, in practice, can avail themselves of this wise permission? The annual shortage of staff in March makes it appear, at that time, as if there is no consultant who is not determined to have his pound of flesh, but this is undoubtedly a mere clinical impression not based on sound statistics. The staffing position in the majority of hospitals in the country does not make the arranging of annual leave an easy matter. Indeed for some of our colleagues it is apparently impossible to arrange anything like an adequate break to permit recuperation from the exhaustion of constant theatre work. It is sincerely to be hoped that the reports of Commissions and Working Parties relating to the conditions of service and staffing will appear during the next year or so and will point the way to a solution of this very real difficulty.

Perusal of Dr. Coope's (1952) excellent little anthology *The Quiet Art* can be depended on to provide food for editorial thought. In these pages will be found an excerpt from Peter Harding's *The Corner of Harley Street,* in which any tendency to cut short holidays is denounced, but is still regarded as preferable to "pollution" by work. "And unless you particularly need them for preserving specimens of the local flora or maintaining the creases upon your Sunday trousers, you should never, never, never pack technical books in a holiday trunk. It is to put poison—or at any rate water—into the wine that you are to pour

[*Continued on page* 198

Brit. J. Anaesth. (1959), **31**, 190

THE EAR OXIMETER AS A CIRCULATORY MONITOR

*II: The Infrared Pulse, a Moment-to-Moment Guide to Cardiac Output**

BY

SEYMOUR SCHOTZ, SHIRLEY S. BLOOM, FREDRICK W. HELMSWORTH, HERBERT C. DODGE AND EDWARD L. BIRKMIRE

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IN an earlier communication (Schotz et al., 1958) we reported our experiences which led us to conclude that the ear oximeter, besides indicating the percentage oxygen saturation of arterialized blood, might also serve as a sensitive circulatory monitor. The purpose of this communication is to report on a further refinement of oximetric recording which we have found quite valuable in evaluating cardiac output.

The ear oximeter functions on the principle that as blood becomes more or less saturated with oxygen its colour changes, and that by measuring this colour change with a sensitive photo-electric device one is able to obtain fairly accurate measurements of blood oxygen saturation. The initial standardization of the modified Wood earpiece eliminates the factors of tissue thickness and pigmentations which might alter the transmission of light (Glasser, 1950). There remain only two factors which affect the transmission of light: (*a*) the oxygen saturation of the blood and (*b*) the amount of blood in the ear.

The earpiece has two separate photocells covered by two different light filters. One cell "sees" light mainly in the red band (at 650 millimicrons), while the other "sees" light mainly in the infrared (I-R) band (at 800 millimicrons). In the single scale ear oximeter, these two outputs are made to buck one another electronically and the resulting output will signify oxygen saturation (Wood, 1950).

We have shown that if the recording for the ear oximeter utilizes the upper 15 per cent of the saturation scale, a pulsating trace is obtained which results from the movement of blood through the ear tissue as the heart goes through its cycles of systole and diastole. If at the same time one taps the output of the infrared cell and records this separately, a much more satisfactory tracing of these pulsations is obtained (fig. 1).†

Several investigators have studied the peripheral circulation with "photo-electric plethysmographs". Matthes et al. (1940) studied the peripheral circulation, and with tambours recorded arterial traces simultaneously with photo-electric traces of the circulation of fingers, toes, and folds of skin. He showed the close correlation between these two traces especially during cardiac arrythmia. Earlier, Bonsmann (1934) succeeded in measuring the blood pressure in rats by shining a light through the tail on to a photo-electric device, compressing the tail proximally, and noting the point at which the pulsating photo-electric output appeared. Hertzmann (1938) studied the circulation in the skin in several areas over the body and reported that the circulation in the ear was exceeded only by that in the finger pad in amplitude of volume pulse. Using a Millikan oximeter, Landis (1948) showed a close and reproducible correlation between the obliteration of ear pulses and loss of consciousness. In a most interesting series of studies Wood et al. (1950), using a specially designed earpiece with only one photocell in the infrared range, showed that

*This work was made possible through a grant-in-aid from Burroughs, Wellcome, Co. (U.S.A.), Inc.

†The instrument used was Wood's absolute reading ear oximeter and the electronic recorder was an ink-writing Grass polygraph equipped with model 5 P1 pre-amplifier.

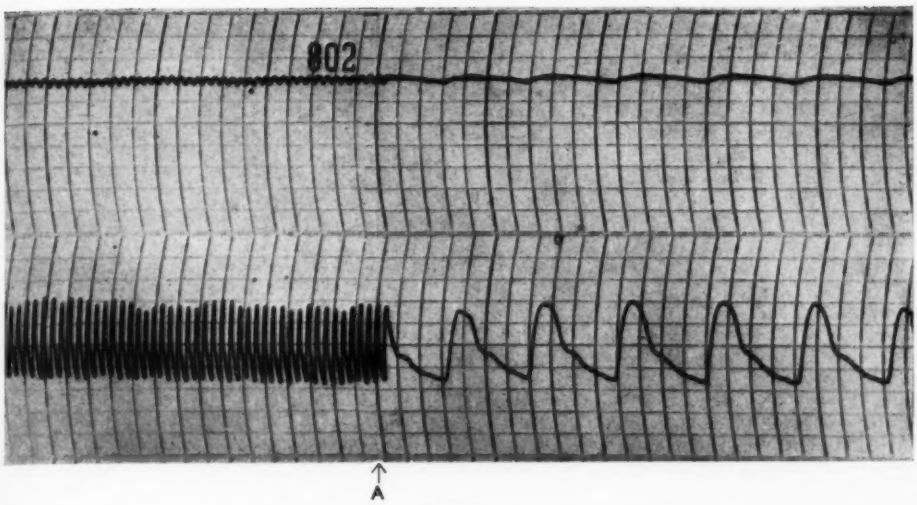

FIG. 1

Normal oximeter and I–R pulse record.
Upper trace: Whole oximeter 100–85%.
Lower trace: Output of I–R cell (I–R pulse)
A—Paper speed changed from 2.5 mm/sec to 25 mm/sec.

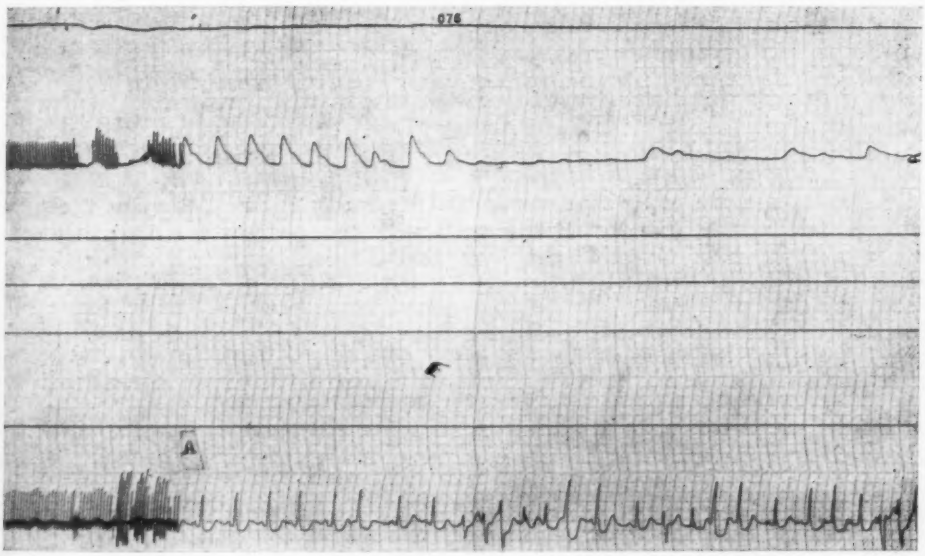

FIG. 2

Oximeter, I–R pulse, and e.c.g. during mitral valvotomy.
Upper trace: Whole oximeter 100–85%.
Middle trace: I–R pulse.
Lower trace: E.c.g.
A—Paper speed changed from 2.5 mm/sec to 25 mm/sec in order to visualize more clearly the e.c.g. complexes. Each small box=5 mm.

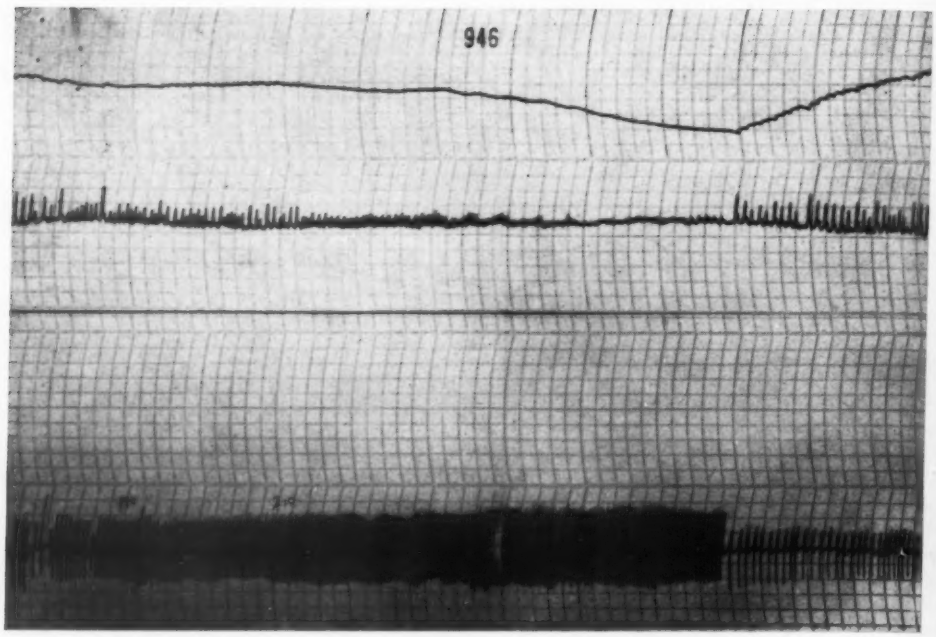

FIG. 3
Oximeter, I–R pulse, and e.c.g. during paroxysmal tachycardia.
Upper trace: Whole oximeter 100–85%.
Middle trace: I–R pulse.
Lower trace: E.c.g.
Paper speed: 2.5 mm/sec.

accurate measurements of arterial blood pressure could be made by this method. Simultaneous tracings made of radial, brachial, and "ear opacity" pulses showed a remarkably close correlation throughout these studies.

For the past year we have been recording the whole oximeter and the output of the infrared circuit simultaneously during a variety of operations on the heart. The method is simple. Just beyond the input to the oximeter control box the infrared circuit is tapped and led into the input of a separate pre-amplifier-amplifier. Thus simultaneous tracings of oximeter and infrared circuit are made. These records tend to substantiate the conclusions reached in our preliminary report.

During finger manipulations of stenotic mitral valves there are often brief periods during which very little blood enters the left ventricle, accompanied by episodes of marked cardiac arrhythmia. The changes in the I-R pulse during these periods are quite striking, as illustrated in figure 2.

During periods of marked tachycardia stroke volume output may fall sharply. Figure 3 illustrates this very well. Note the marked narrowing of the I-R pulse during the period of 210 beats per minute and the instant change when a much slower rate spontaneously occurs. In figure 4 the changes noted during a period of in-and-out of ventricular fibrillation are illustrated. Note the instant fall in the I-R pulse at the start of ventricular fibrillation and the instant return as the normal rhythm returns.

The changes in stroke volume output which may occur when the surgical correction of stenotic or incompetent heart valves are performed are often quite striking. In figure 5 the pressures in the aorta and left ventricle are alternately re-

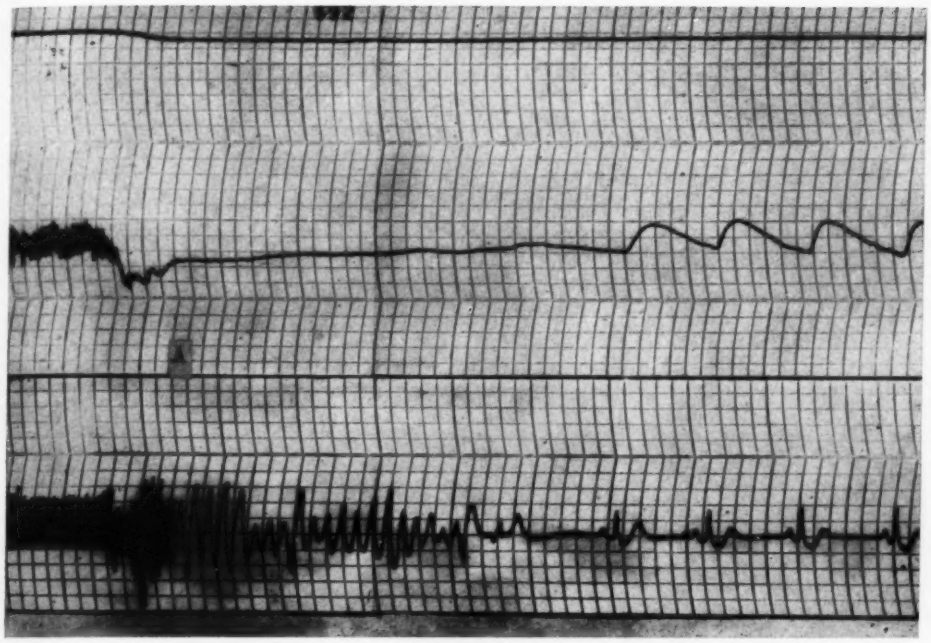

FIG. 4
Oximeter, I–R pulse, and e.c.g. during ventricular fibrillation.
Upper trace: Whole oximeter 100–85%.
Middle trace: I–R pulse.
Lower trace: E.c.g.
A—Paper speed changed from 2.5 mm/sec to 25 mm/sec to better visualize the e.c.g.
Each small box=5 mm.

corded. The scale indicates a differential of 70 to 75 mm Hg across the aortic valve. Figure 6 illustrates the change after aortic valvotomy. The differential has fallen to 15 mm Hg. Figure 7 illustrates the change in I-R pulse which accompanied the aortic valvotomy. The changes in forward stroke volume output incident to surgical correction of an incompetent mitral valve are illustrated in figure 8. The immediate effect upon the dynamics of blood flow is easily discernible. A similar change in the dynamics of blood flow can be seen in figure 9, resulting from the surgical correction of a very tight mitral stenosis. Tracings made before and after the commissurotomy are put side by side and show the distinct improvement in what must be ventricular filling and output.

During periods of coughing and straining the rise in intrathoracic pressure may alter cardiac filling and output. Figure 10 illustrates just such an effect by the irregularity of the I-R pulse.

The slowing in heart rate and the improvement in stroke volume output which accompanies adequate digitalization is illustrated in figure 11. This is a composite photograph of the I-R pulses made at the start of digitalization, 13 minutes and 32 minutes after the administration of 0.8 mg of Cedilanid to a patient in uncontrolled atrial fibrillation. It is interesting to note that whereas the change in stroke volume between 8.48 and 9.01 may be explained purely on a slowing in rate, the further improvement at 9.20 took place without any further slowing (indeed, the rate is slightly faster), indicating a change in

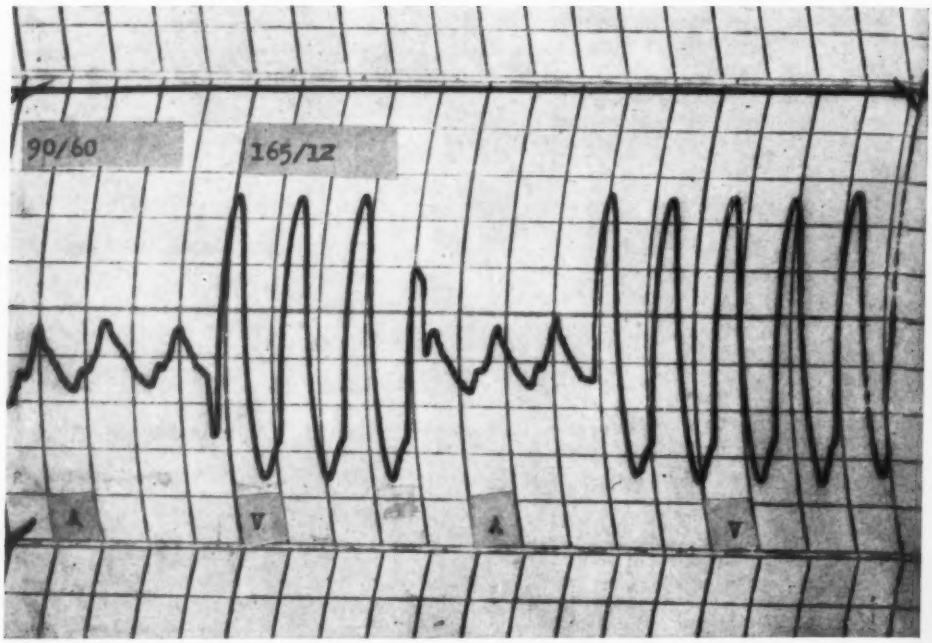

FIG. 5

Pressure recordings in the aorta and left ventricle alternately, before valvotomy.
A—Aorta. V—Left ventricle.
Each small box of 5 mm equals 25 mm Hg pressure.

the force of the heart beat probably resulting from the shortening of muscle and more effective contraction.

COMMENT

The foregoing illustrations seem to point to the I-R pulse as a convenient device for evaluating changes in cardiac stroke volume output. It may be argued that all we are doing is recording a tissue perfusion pulse and that other factors such as vasoconstriction and preferential circulation to other organs may significantly alter the interpretations we should give to these recordings. In the matter of vasoconstriction we are accumulating evidence which we plan to publish at a future date which tends to show that once the ear has been adequately warmed by the heat of the earpiece lamp, the small vessels of the ear do not readily respond to vasoconstrictors. It is possible, however, that vasomotion in other areas of the body may shift a significant enough volume of blood so that the amount circulating towards the ear is increased or decreased as the case may be. The final answer to this question will have to await further work to be done towards quantitating these I-R pulses with standard methods of determining cardiac output. For the time being, however, the foregoing illustrations together with direct observations of the heart have impressed us with the very close correlation between the action of the heart and the changes in the I-R pulse waves. Even without a method of quantitating these pulses, merely using the patient as his own control, we have a guide as to the state of the circulation which we have found as important as an intra-arterial recording with the additional advantage that it is far easier to set up, and there is no needle or catheter to become plugged.

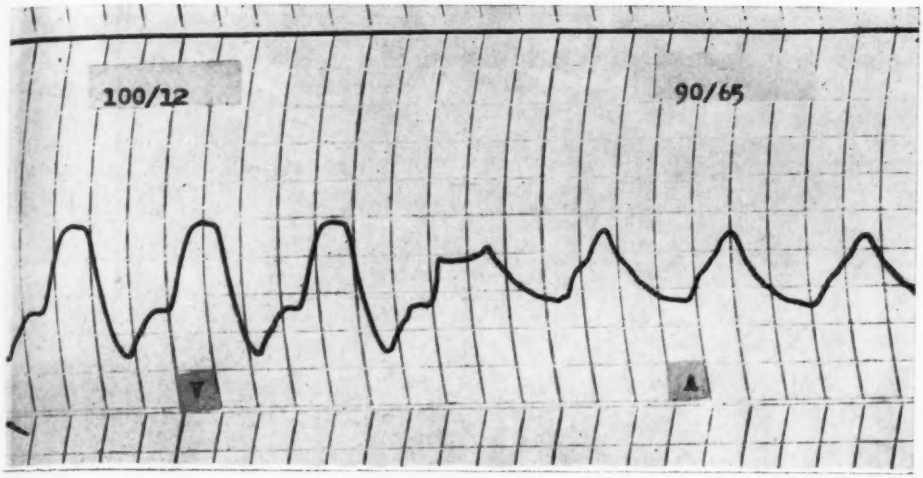

FIG. 6
Same as figure 5 after aortic valvotomy.

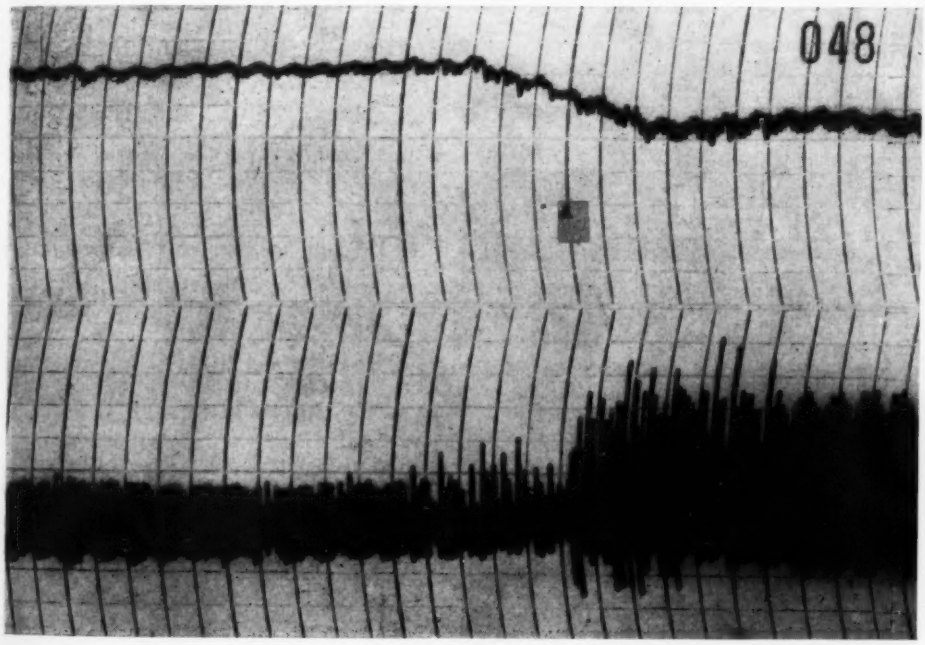

FIG. 7
Oximeter and I–R pulse during aortic valvotomy.
Upper trace: Whole oximeter. Lower trace: I–R pulse.
A—Valvotomy performed.

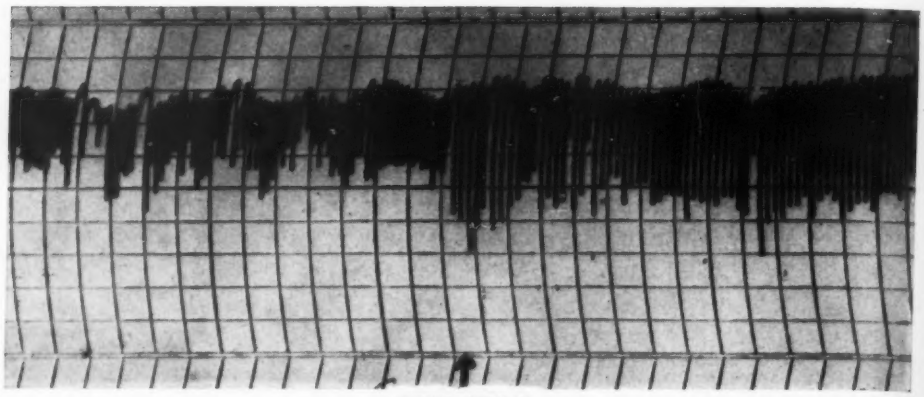

FIG. 8
I-R pulse during tying of the circumferential suture for a. mitral insufficiency.

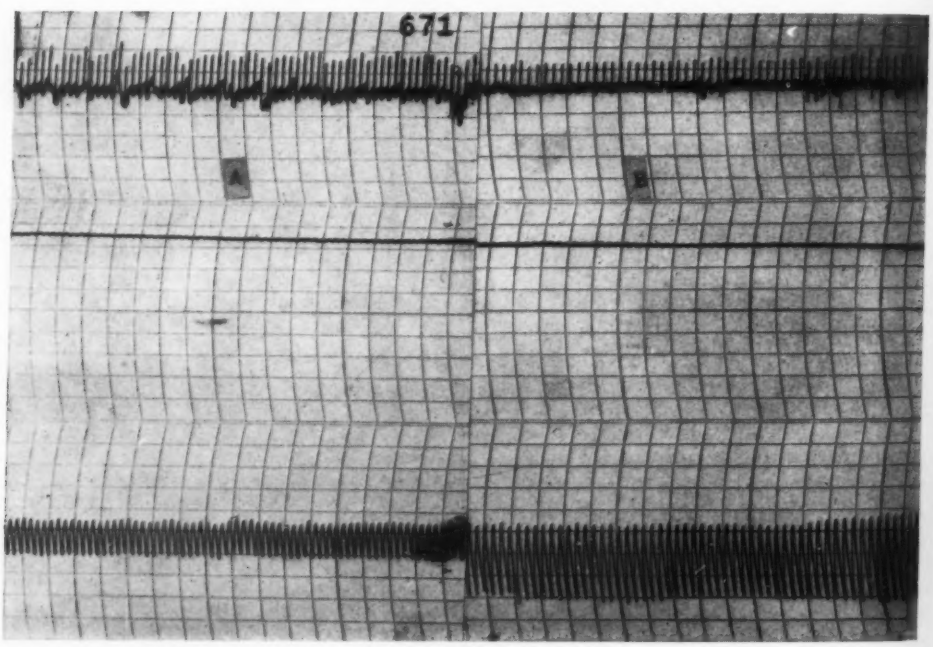

FIG. 9
Before (A) and after (B) mitral valvotomy.
Upper trace: E.c.g.
Middle trace: Whole oximeter 100–85%.
Lower trace: I–R pulse.

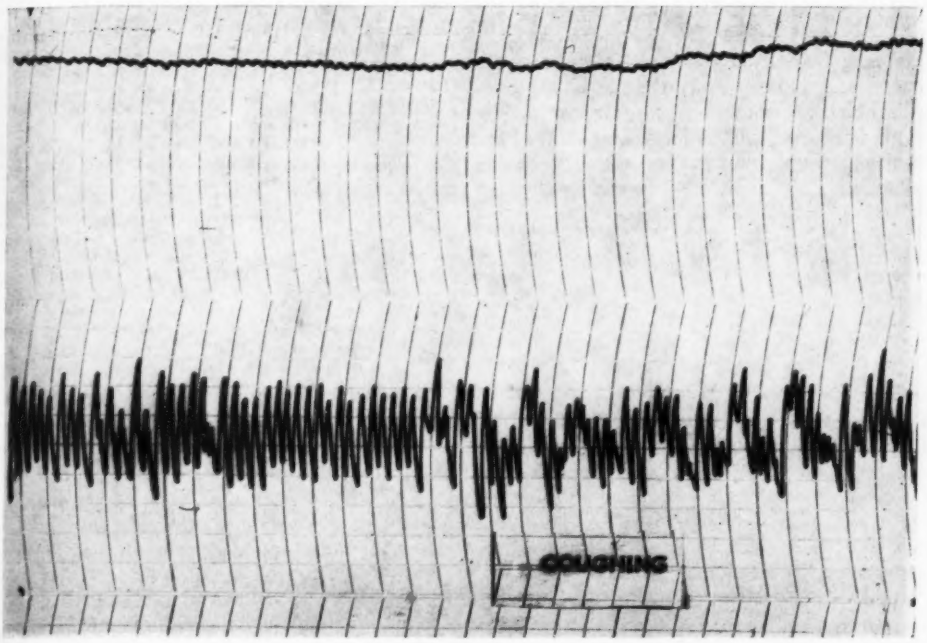

FIG. 10
Valsalva effect produced by coughing.
Upper trace: Whole oximeter 100–85%. Lower trace: I–R pulse.

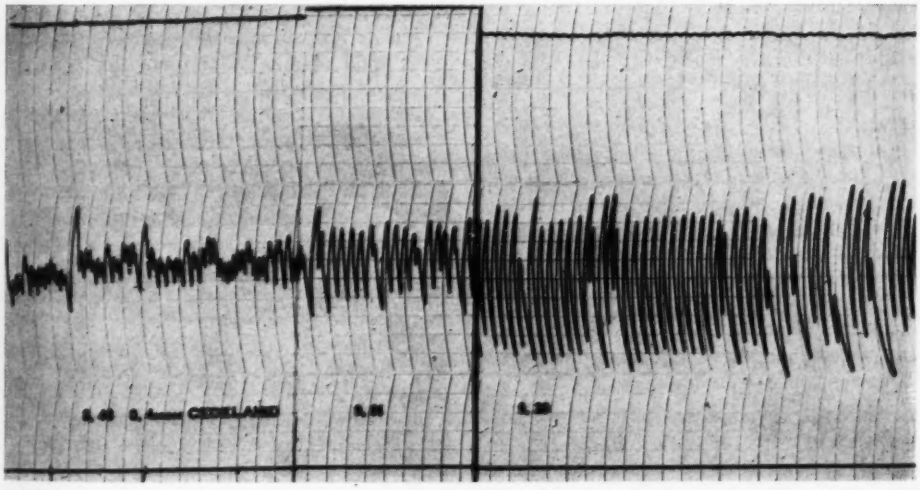

FIG. 11
Effect of Cedilanid on I–R pulse.
Upper trace: Whole oximeter 100–85%. Lower trace: I–R pulse.

SUMMARY

By tapping the infrared circuit of a standard ear oximeter and making it record separately, a tracing is obtained which seems to follow closely changes in cardiac stroke volume output. We have presented several illustrations which seem to substantiate this as a very useful system of monitoring the circulation.

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EDITORIAL *continued from page* 189

out before the gods of mountain and moor and loch."

Finally we cannot give better advice to our colleagues than that entailed in a letter by the wise Dr. Johnson as reported by Boswell:

Dear Sir,

I am much pleased that you are going a very long journey, which may by proper conduct restore your health and prolong your life.

Observe these rules:

1. Turn all care out of your head as soon as you mount the chaise.
2. Do not think of frugality; your health is worth more than it can cost.
3. Do not continue any day's journey to fatigue.
4. Take now and then a day's rest.
5. Get a smart sea-sickness, if you can.
6. Cast away all anxiety, and keep your mind easy.

This last direction is the principal; with an unquiet mind, neither exercise, nor diet, nor physick can be of much use.

I wish you, dear Sir, a prosperous journey and a happy recovery.

I am, dear Sir,

Your most affectionate, humble servant,

Sam. Johnson.

July 28, 1782.

(Boswell, *Life of Johnson*)

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Brit. J. Anaesth. (1959), **31**, 199

HYPOTENSION DUE TO HALOTHANE

BY

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IN the pharmacological section of the report to the Medical Research Council on Fluothane by the Committee on Non-explosive Anaesthetic Agents (1957), the conclusion was drawn that the hypotensive action was made up of a central depressant action, together with some weakening of the heart and possibly a small contribution of peripheral ganglion block. One further possibility remained which had not been thoroughly examined, namely that halothane might have a direct relaxing action on the smooth muscle of the arteries. We have therefore carried out some observations to test whether such an action was exerted, and in addition have made observations on the spleen and on the intestines.

METHODS

Experiments were performed in which the hind leg of a dog was perfused with blood made incoagulable with heparin. One dog was anaesthetized with ether, after which tracheotomy was performed and cannulae were inserted in the left common carotid artery and in the right external jugular vein. The dog was then bled into a polythene beaker containing heparin, 800-900 ml being collected. The front part of the bony thorax was removed and cannulae were tied into the pulmonary artery and into the left auricle. A ligature was tied round the ventricle near its base. Blood was then pumped from a Dale-Schuster pump into the pulmonary artery while the lungs were ventilated with oxygen and 5 per cent carbon dioxide. The blood leaving the left auricle was collected in a reservoir and, until the second dog was prepared, was recirculated through the lungs.

The second dog was also anaesthetized with ether, a tracheal cannula and a carotid cannula were inserted, and about 150 ml blood was withdrawn for addition to the blood reservoir. The dog was then eviscerated and cannulae were tied in the external iliac artery and vein of one side pointing towards the aortic bifurcation. The aorta was ligatured below the origin of the external iliac arteries, and ligatures were passed round the aorta and vena cava just above the bifurcation. At a given moment these ligatures were tied and perfusion was begun from the Dale-Schuster pump through the cannula in the external iliac artery from which blood passed to the leg of the opposite side. The venous effluent from the leg was passed to an outflow recorder and was carried to the reservoir from which it was pumped once more through the lungs. A side arm of the cannula tied in the external iliac artery was connected to a mercury manometer. In this way the resistance to flow of the leg vessels was recorded, as well as the venous outflow. In other experiments observations on spleen volume were made in spinal cats which were prepared by cutting the cord at the second cervical vertebra under ether anaesthesia. The spleen was brought out through the body wall on the left side and placed in a plethysmograph so that variations in its volume could be recorded.

In other experiments observations on intestinal motility were made in spinal cats. An incision was made into the upper end of the jejunum through which was inserted a small balloon attached to the end of a catheter. The balloon was then pushed up into the duodenum. The balloon and catheter

had been filled with water, and the contractions of the duodenum were transmitted to a piston recorder.

In order to administer halothane or ether, the outlet from a Palmer "Ideal" pump was connected by tubing to a T-adaptor close to the tracheal cannula. The appropriate quantitative inhaler was connected to the intake of the pump and the tubing mentioned above was kept fairly narrow in order to reduce the time lag between altering the setting of the concentration control and the arrival of the new mixture in the lungs. The expirations were led from the side branch of the T-adaptor through the mechanical valve on the pump onwards through an exhaust tube to the outer air.

In all experiments the rotary drive to the pump was set to a fixed rate of inflation—25 per minute. The stroke volume was adjusted according to requirements to a few spaced values: 100 ml, 150 ml and 200 ml. The peak inflation pressures were recorded on a dial manometer in a side branch of the tubing leading to the tracheal connector. For cats, the peak inflation pressures were in the region from 9 to 15 cm H_2O for tidal volumes of 100 to 150 ml. Often a deterioration of the preparation was apparent from a steadily rising inflation pressure while the tidal volume remained unaltered.

When halothane was used the apparatus connected to the intake of the pump was a modified E.M.O. halothane inhaler. It had been modified so that even for the low minute volumes ($2\frac{1}{2}$ litres) used the concentrations delivered were not far away from the settings of the control for human anaesthesia. The inhaler had been calibrated in the laboratory with a similar Palmer pump. Variations in output were reduced to a small value by immersing the inhaler in a water bath, although it contained the usual thermo-compensator, which automatically reduces effects of external temperature fluctuations. The range of halothane concentrations available from this inhaler was up to 4 per cent by volume.

For ether an Oxford vaporizer, modified for animal work, was attached to the intake of the pump, although a standard ether E.M.O. inhaler would have been equally suitable. The range of concentrations which can be delivered from the latter apparatus is up to 20 per cent by volume.

RESULTS

Observations in the perfused hind leg

In the course of experiments in which the hind leg of a dog was perfused with blood by way of a cannula tied in the left external iliac artery, we observed the effect of ventilating the lungs with 1.5 per cent halothane. Figure 1 illustrates the effect. The upper record is that of the venous outflow from the common iliac vein, and when halothane was administered the outflow increased. The lower record is that of the pressure in the perfusion cannula, and when halothane was administered the pressure fell because the arterial resistance diminished. The pressure recovered when halothane was stopped and the venous outflow declined. The results in two experiments in which halothane was compared with ether are given in table I. .

TABLE I

Anaesthetic		Duration (min)	Fall in arterial resistance (mm)
Exp. 1			
(*a*) Halothane	1.5%	5	170 to 132
(*b*) Halothane	1.5%	5	153 to 119
(*c*) Ether	6.0%	5	no fall
Exp. 2			
(*a*) Halothane	2.0%	4	119 to 98
(*b*) Ether	8.0%	4	106 to 100

Observations on intestinal contractions

The effects of halothane and of ether on intestinal contractions recorded by a balloon in the duodenum are shown in figure 2. The adrenal glands were excluded from the circulation. The contractions were vigorous because of the injection of 0.1 mg eserine sulphate 30 minutes previous to the taking of the record. During the administration of halothane, 0.7 per cent, there was complete inhibition of the contractions. During the administration of ether, 10 per cent, there was no inhibition. Three experiments were performed with a similar result, although the difference between halothane and ether was greatest in the experiment of figure 2.

Observations on spleen volume

The sympathetic nerves to the spleen accompany the arteries, and impulses passing along

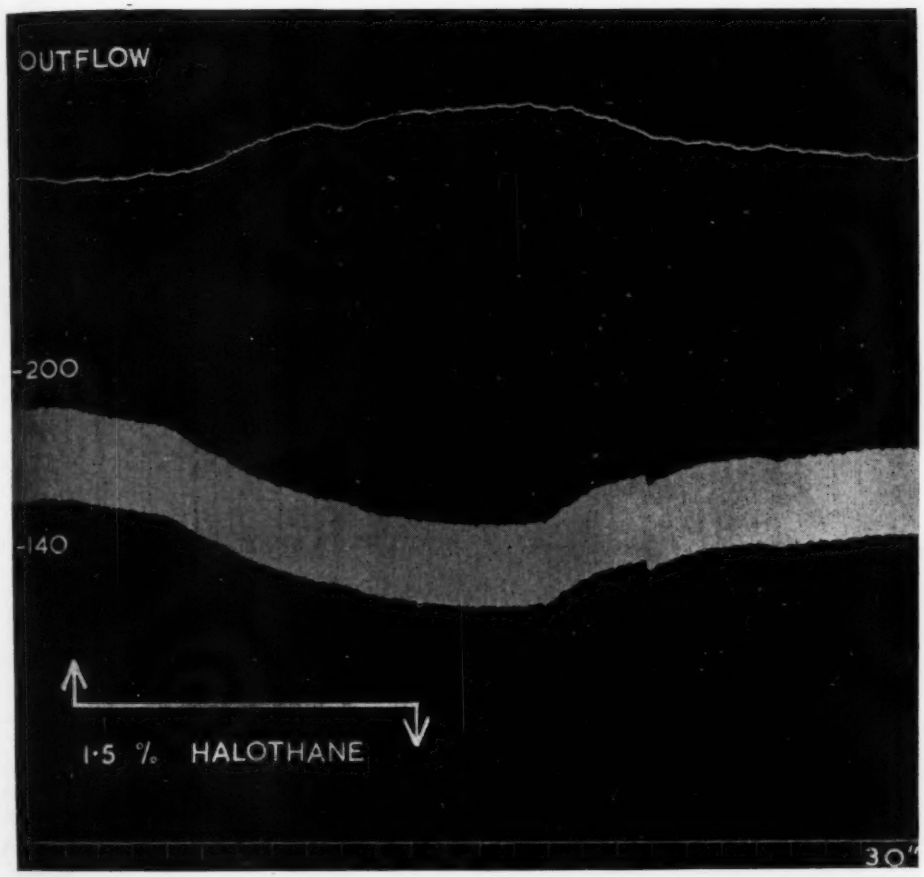

FIG. 1

Record from an experiment in which the hind leg of a dog was perfused with blood. The blood on leaving the leg was pumped through the lungs of another dog which were ventilated with O_2 and 5 per cent CO_2. The blood was then pumped back to the leg. When halothane was added to the ventilating mixture in 1.5 per cent concentration, the arterial resistance in the leg fell, and the outflow from the leg increased.

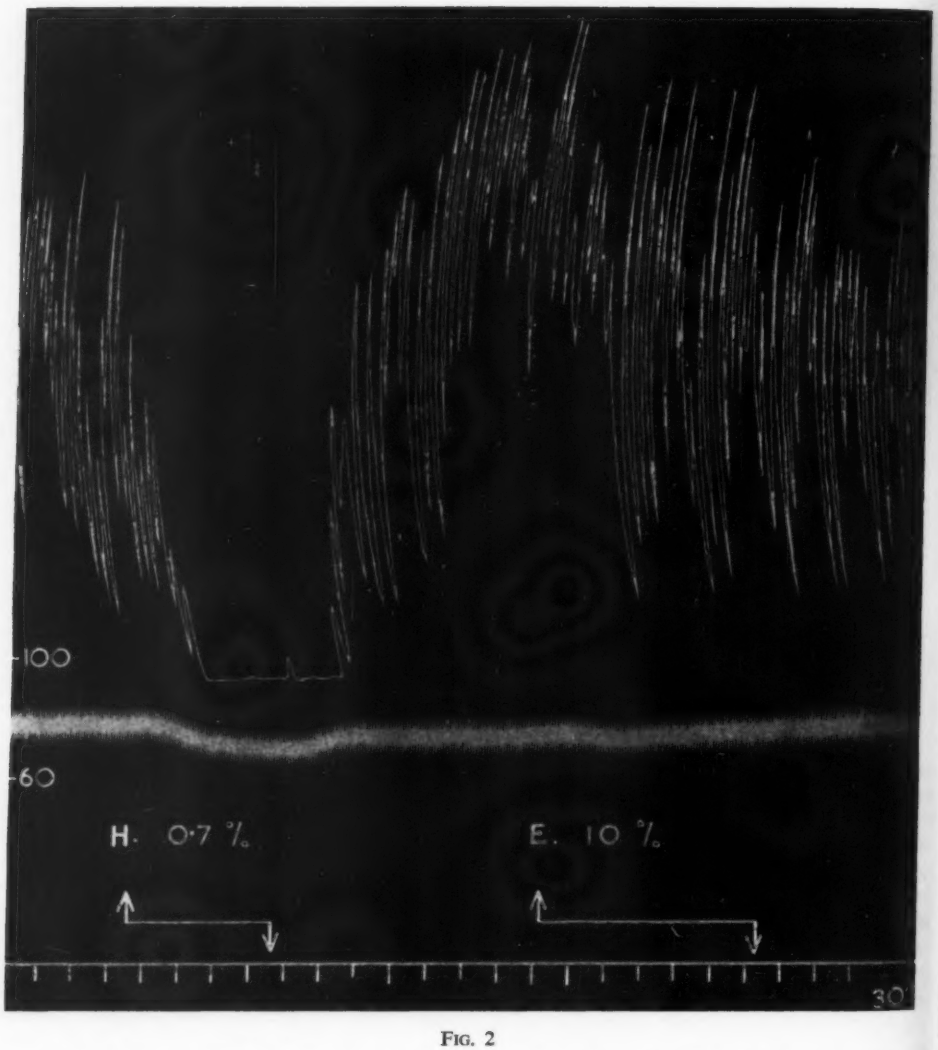

FIG. 2

Record from an experiment in a spinal cat in which the contractions of the duodenum were recorded from a balloon inside it. The adrenal glands were excluded. When the cat was ventilated with halothane 0.7 per cent the contractions were arrested. When the cat was ventilated with ether 10 per cent the contractions were not arrested.

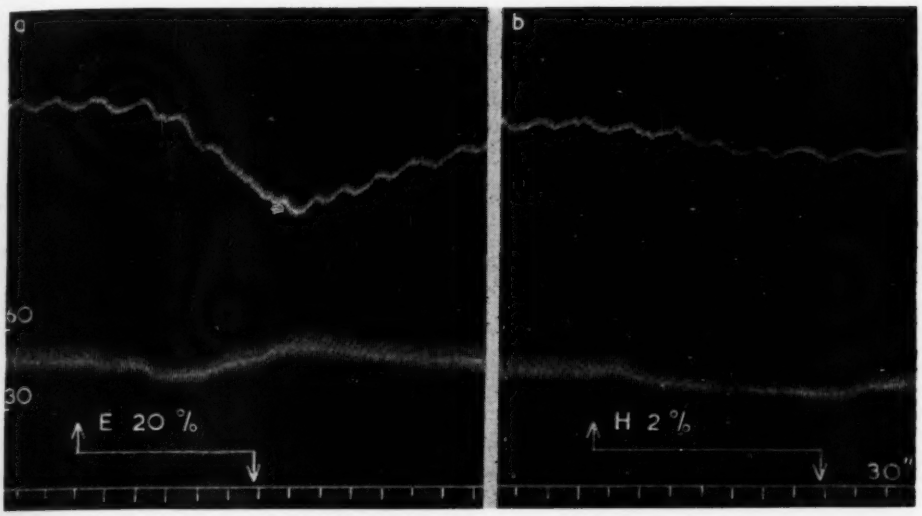

FIG. 3

Record from an experiment in a spinal cat in which the spleen volume was recorded. The adrenal glands were excluded. When the cat was ventilated with ether 20 per cent, the spleen contracted and the volume fell. When the cat was ventilated with halothane 2 per cent, there was a very slight fall in the spleen volume.

them cause the spleen volume to shrink. Figure 3 shows in (*a*) the effect of ventilating a spinal cat with ether, 20 per cent by volume. The adrenal glands had been excluded. The blood pressure was low and was not affected, but the spleen volume declined during administration of ether, recovering again when ether was discontinued. In figure 3 (*b*) halothane was given in 2.5 per cent concentration. The volume record was slowly rising, and when halothane was given there was a slight fall, the volume recovering when halothane was discontinued. Similar results to this were obtained in three other experiments. The conclusion was drawn that under ether the sympathetic impulses to the spleen were increased and as a result the volume diminished. Under halothane there was also some diminution in volume but it was much smaller. Either the increase in sympathetic impulses was much less under halothane, or the impulses were counteracted by a direct action on the spleen, causing relaxation.

DISCUSSION

The observations on the intestine and on the perfused vessels of the hind leg indicate that halothane has an inhibitory action on smooth muscle greater than that of ether, even when given in a concentration of less anaesthetic potency. Ether has previously been shown to cause contraction of the spleen volume (Bhatia and Burn, 1933) and this effect indicates that ether causes an increase in the flow of sympathetic impulses since it occurs when the adrenal glands are excluded. Halothane was observed to have some effect in causing contraction of the spleen but usually less than ether, as shown in figure 3. In one experiment it was recorded that a contraction of the spleen began when halothane was given, but ceased and the spleen dilated while halothane was still acting. This observation suggested that there were two effects; first, contraction due to increased sympathetic impulses, and then dilatation because the sympathetic action was overcome by direct action on the muscle.

When all the results are taken together they point to halothane having a relaxing or dilating action on the smooth muscle of the vessels, of the spleen and of the intestine, from which the conclusion may be drawn that the fall in blood pressure during halothane anaesthesia is in part, at least, due to this direct effect. The observations on the spleen suggest that sympathetic impulses are increased, although not to the same extent as they are under ether. The inhibition of the intestine could indeed be sympathetic in origin.

SUMMARY

Halothane has a direct relaxing action on smooth muscle which probably contributes to its action in lowering blood pressure.

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ATROPINE AS AN ANTISIALOGOGUE, COMPARED WITH L-HYOSCYAMINE (BELLAFOLINE), SCOPOLAMINE BUTYLBROMIDE (BUSCOPAN) AND OXYPHENONIUM (ANTRENYL)

BY

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THE belladonna alkaloids are commonly used in anaesthetic premedication because of their ability to depress salivary activity. This effect is achieved by blocking the response to acetylcholine at the effector organs innervated by postganglionic cholinergic fibres. The drug which is best known and most commonly used is atropine. In recent years another drug of the belladonna alkaloids group has been introduced as an antisialogogue, namely l-hyoscyamine (Bellafoline, Sandoz), a preparation which contains the pure laevorotatory alkaloids of belladonna leaves. Griggs, Adriani and Berson (1953) reported that l-hyoscyamine was clearly superior to atropine as a depressor of salivary activity—a conclusion based on their clinical experience. Their finding was confirmed by other authors using more objective methods (Galloon, 1956; Wyant and Dobkin, 1957). Galloon compared the effect of atropine and l-hyoscyamine by stimulating salivary secretion with lemon juice and collecting the saliva in a measuring cylinder. Wyant and Dobkin stimulated the secretion by injection of carbaminoylcholine chloride (Carbachol), and collected the parotid secretion by means of a plastic suction cup applied to the opening of Stensen's duct.

Our experience with anticholinergic drugs in the treatment of poisoning indicated that atropine was the most active antidote (Diamant, 1954). Its excellent effect as an antisialogogue was then observed but was not measured exactly. In subsequent experiments, using an exact method for stimulation of the salivary flow, the antisialogogue action of atropine was studied (Diamant and Holmstedt, 1957). Since the results were inconsistent with the conclusions both of Galloon and of Wyant and Dobkin, it was thought worth while to compare atropine with l-hyoscyamine and two other widely used anticholinergic preparations—scopolamine butylbromide and oxyphenonium—using the method of Diamant, Diamant and Holmstedt (1957).

MATERIAL AND METHODS

Eight patients were selected, ranging in age from 33 to 50, and having no disturbances of the salivary glands or disorders of the circulatory system. The technique, described by Diamant, Diamant, Holmstedt (1957), consists of stimulation of the salivary secretion by intravenous infusion of acetyl-β-methylcholine iodide (Betacholyl; Vitrum) in 0.02 per cent solution. This will be referred to hereafter as methacholine. The infusion is given over two 5-minute periods separated by an interval of 5 minutes. The antisialogogue agent is administered by slow intravenous injection 1 minute after the beginning of the second infusion period. The latter is followed by 5 minutes' rest and a third infusion period. Throughout the experiment the pulse rate is registered by an automatic electrocardiographic recorder ad modum Johanssen (1958). Figure 1 shows a typical experimental chart.

Drugs.

The drugs used were as follows:

(1) Atropine sulphate 0.05 per cent solution

(1 ml = 0.5 mg) in a dose of 0.5 mg in all experiments except one, in which 1 mg was used.

(2) l-Hyoscyamine (Bellafoline, Sandoz) in doses ranging from 0.05 mg to 0.5 mg.

(3) Scopolamine butylbromide (Buscopan, B.C.H. Boehringer Sohn) in a dose of 20 mg.

(4) Oxyphenonium (Antrenyl bromide, Ciba) in a dose of 1 mg.

In all experiments the above doses were given regardless of body weight (table I).

RESULTS

Atropine.

Atropine was used in each of the nine cases, the dose being 0.5 mg in eight and 1 mg in one. In all experiments the typical excellent antisialogogue effect of atropine was noted. The pulse rate, which was raised by the infusion of methacholine, dropped after the injection of atropine and remained normal during the second rest period as well as the third methacholine infusion period. In the patient in whom 1 mg of atropine was injected, the pulse rate fell to normal after the injection of atropine. However, it rose again, and remained at a fairly high level as a sign of slight atropine overdosage. These observations were in agreement with earlier experiments (Diamant and Holmstedt, 1957).

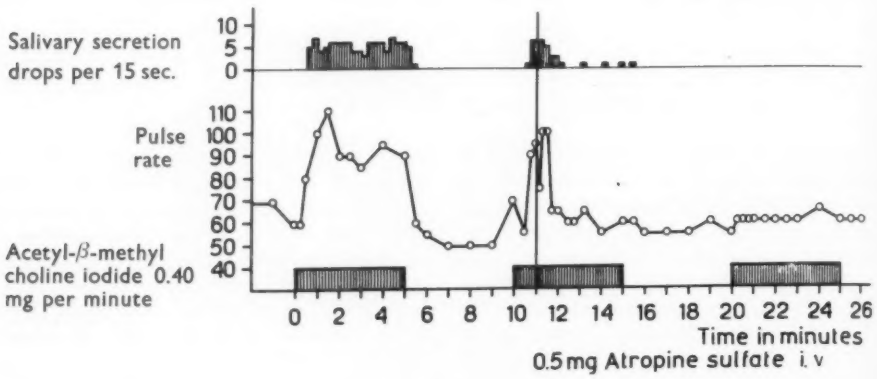

FIG. 1

Typical chart showing the effect of atropine on the pulse rate and the salivary secretion using the method described by Diamant et al. (1957).

TABLE I

Distribution of injections of antisialogogue drugs

Case	Atropine	l-Hyoscyamine	Oxyphenonium	Scopolamine butylbromide
1. E.W.	1	1	–	1
2. G.K.	1	1	1	1
3. T.Ö.	1	1	1	1
4. S.T.	1	1	–	1
5. D.W.	1	1	–	–
6. E.J.	1	1	1	–
7. A.E.	1	2	–	–
8. E.K.	2	2	–	–

l-Hyoscyamine (Bellafoline).

l-Hyoscyamine was used in all subjects, though in varying amounts. In five cases in which 0.5 mg was injected the antisialogogue effect was excellent. Where 0.3 mg was administered, the effect on the salivary secretion was good, but in two other cases in which the dose was 0.1 mg and 0.125 mg respectively the corresponding effect was very slight. In four of the five patients who received 0.5 mg, the pulse rate rose and had not returned to normal 30 minutes after the end of the methacholine infusion, a fact which pointed

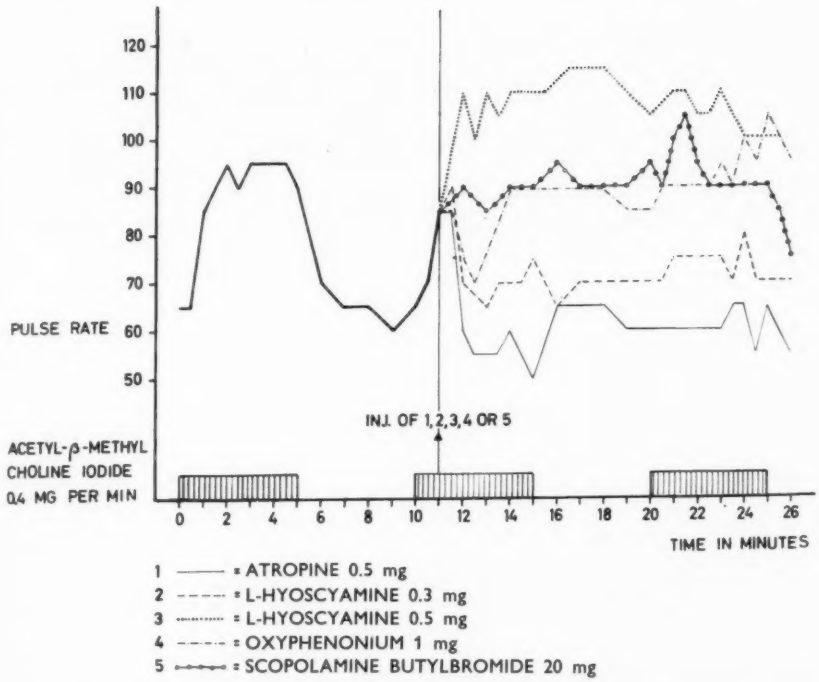

FIG. 2

Effect of atropine, l-hyoscyamine, oxyphenonium and scopolamine butylbromide on the pulse rate in cases where intravenous infusion of methacholine iodide has been given.

to slight overdosage (fig. 2). In the five cases in which 0.3 mg or less of l-hyoscyamine was injected, no toxic effect on the circulation was noted.

Oxyphenonium (Antrenyl bromide).

In three patients oxyphenonium was used in a dose of 1 mg and had a very good antisialogogue effect. In one of them a major rise in the pulse rate was observed.

Scopolamine butylbromide (Buscopan).

This substance was used in four experiments. The salivary secretion was but little affected and there was an evident, though not marked, effect on the pulse rate.

DISCUSSION

Atropine compared with l-Hyoscyamine.

As illustrated by table II, atropine in a dose of 0.5 mg was invariably effective as an antisialogogue without producing any toxic side effects. It should be pointed out that the duration of the relevant action was recorded only for 30 minutes after injection of the antisialogogue. The same doses of l-hyoscyamine also had a good antisialogogue effect. No difference was found between the two drugs in their effect on the salivary secretion.

Doses of 0.5 mg atropine and 0.3 mg l-hyoscyamine were almost equivalent in their antisialogogue action; the same applied to 1 mg atropine and 0.5 mg l-hyoscyamine (fig. 2). As regards the side effects of the two drugs, 0.5 mg l-hyoscyamine (the contents of one ampoule) raised the pulse rate, as a sign of slight overdosage. The same was true in most subjects tested with 1 mg atropine, as shown by Diamant and Holmstedt (1957, 1959), and in one of our cases. We used the intravenous route in all our experi-

TABLE II

Effect on the pulse rate and the salivary secretion of atropine, l-hyoscamine, oxyphenonium and scopolamine butylbromide counteracting intravenous infusion of methacholine iodide.

	Atropine				l-Hyoscamine										Oxyphe-nonium		Scopo-lamine butyl-bromide	
	0.5 mg		1.0 mg		0.05 mg		0.1 mg		0.125 mg		0.3 mg		0.5 mg		1.0 mg		20.0 mg	
	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)
1 E.W.	−	++											+	++			(+)	(+)
2. G.K.	−	++											(+)	++	−	++	(+)	(+)
3. T.O.	−	++											−	++	−	++	(+)	(+)
4. S.T.	−	++											+	++			+	(+)
5. D.W.	−	+							−	++								
6. E.G.	−	++					−	(+)							+	++		
7. A.E.	−	++			−	−	−	(+)										
8. E.K.	−	+	(+)	++							−	++	+	++				

− = no
(+) = slight
\+ = considerable
++ = marked

(a) overdosage affecting the pulse rate
(b) antisialogogue effect exerted on the salivary secretion.

ments, since with that mode of administration there was no need to consider all the absorption factors associated with the intramuscular or subcutaneous routes. Other experiments have shown that the effects of atropine administration other than intravenous are far more varied (Diamant and Holmstedt, 1959).

As far as can be judged from our experiments l-hyoscyamine is in no way superior to atropine as an antisialogogue. On the contrary, there is a chance of overdosage, since l-hyoscyamine is produced in ampoules of 0.5 mg.

Atropine in comparison to Oxyphenonium and Scopolamine butylbromide.

Oxyphenonium and scopolamine butylbromide were used only in seven experiments. Oxyphenonium was evidently an excellent antisialogogue, and small doses would probably be as good as atropine. Yet even with this compound there is a risk of overdosage that is not offset by any advantage over the action of atropine (fig. 2).

In our experiments we did not consider the duration of action of the drugs. Nevertheless, we feel that during a long operation repeated injections of an antisialogogue are necessary. Other experiments have shown that injected atropine has an effect lasting some 40 minutes. Thereafter a second, smaller, dose should be injected.

Scopolamine butylbromide is a rather weak anticholinergic drug with respect to its action on the salivary glands; but even in the fairly small doses used in our experiments it has a marked action on the pulse rate. This, in conjunction with its slight antisialogogue effect, makes it unsuitable as an anaesthetic premedicant.

CONCLUSIONS AND SUMMARY

As far as can be judged from our experiments which, though relatively few, seem conclusive, atropine has a very good antisialogogue action in doses which produce no toxic effects. None of the other drugs with which it was compared, i.e., l-hyoscyamine, scopolamine butylbromide and oxyphenonium, was found superior to atropine. Hence, there seems no reason to replace it with any of the other drugs here tested.

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SOME DETAILS OF A TECHNIQUE FOR HYPOTHERMIA

BY

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WHILE the technique for hypothermia used experimentally and clinically here over the last five years is largely that of surface cooling as described by Swan et al. (1955), certain modifications and refinements have been evolved which may be of interest to others who use this technique. Routine electro-encephalographic and electrocardiographic recordings have been made, and it is now possible to form some estimate of the value of such recordings.

The cases for which hypothermia is being used can be divided into two classes:

(1) Cases where the circulation to vital centres is for a time to be cut off completely or greatly reduced, e.g. intracardiac manipulation or carotid embolectomy.

(2) Cases where the circulation is not to be cut off completely, but where the patient is already suffering from some hypoxia, and it is thought that hypothermia would improve the chances of recovery after the operation, e.g. operations for tricuspid atresia or very severe mitral stenosis.

Although hypothermia is obviously essential for the first type of case, its reliability and safety is encouraging us to use it more freely for the second type.

Hypothermia has been used for a diversity of cases, so no significant analysis of results can be presented in this paper, in which are considered some points in the technique as seen from the anaesthetist's point of view.

The adult patient is premedicated with pethidine 50–100 mg and atropine 1/200 grain (0.3 mg) intramuscularly 1 hour before operation: the child with chloral hydrate 6 grains (400 mg) per stone (6.3 kg) of body weight, by mouth, 2 hours before operation, and atropine 1/300 grain (0.2 mg) to 1/200 grain (0.3 mg) intramuscularly half an hour before operation. The adult is anaesthetized with the smallest dose of thiopentone (25–100 mg) sufficient to prevent his objecting to a facepiece, and N_2O and O_2. He is also given a small dose of pethidine (20 mg) intravenously to potentiate the N_2O and O_2 during the comparatively long time required for the N_2O to achieve its maximum effect (Gray, 1954). Children are induced with N_2O and O_2, and then for the same reason as above are given 5 mg of pethidine per stone (6.3 kg) intravenously, the exact dose depending on the build and general health of the child. Maintenance in all cases is with N_2O and O_2, and d-tubocurarine is given in doses sufficient to cause full paralysis. The patient is then intubated and put on to a Clutton-Brock respirator (Clutton-Brock, 1957).

The anaesthesia used is as light as possible, and in most cases is insufficient to cause the disappearance of the alpha rhythm as seen on the electroencephalogram (fig. 1). It is not believed that the e.e.g. will give any reliable indication of consciousness or unconsciousness under these conditions (Clutton-Brock, 1958); but the presence of the alpha rhythm, at least indicates that the anaesthetic is light.

When the anaesthetic preliminaries have been completed the patient is put into a bath filled with cold tap water at 10–20°C. Even at 20°C, ice is not added unless the patient is fat, in which case the water is cooled to 10–15°C. Electrocardiographic leads using hypodermic needles (No. 16) are inserted into the arms at this stage. Adequate stirring of the bath water is achieved by a submersible low voltage (12 v.) pump (obtained as government surplus for 25*s*.). This was at first worked off a 12-volt car battery, but latterly a mains unit comprising a transformer and rectifier has been used (also obtained as government sur-

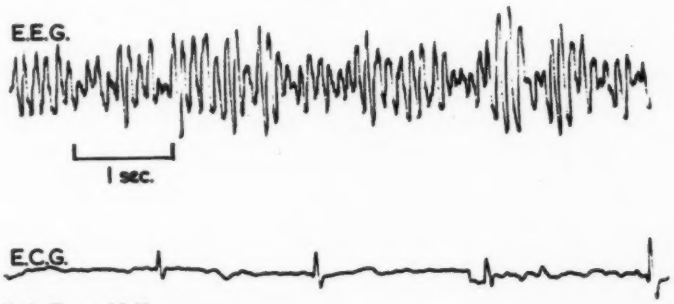

FIG. 1

Electroencephalogram of patient anaesthetized with N_2O and O_2 for cardiac surgery under hypothermia. The depth of anaesthesia is insufficient to abolish the alpha rhythms. (Parieto-occipital lead.)

plus and at a cost of a few pounds). The turbulence of the water produced by this pump is shown in figure 2.

FIG. 2

Showing turbulence of bath water produced by submersible low voltage pump.

Unless the subject is very fat quite rapid cooling is obtained with uncooled tap water under these conditions (fig. 3). For example, it will be seen that the patient in figure 3, who was of average build, was only in the bath for just over half an hour.

We believe that avoiding the use of ice causes less vasoconstriction, and the danger of frostbite to the extremities is reduced. We have also gained the very strong impression that the after-drop, when the patient is removed from the bath, is less.

The efficiency of moving water in changing the temperature of even a hairy animal (unshaved goat) is shown in figure 4. In one experiment the circulation of the water was stopped and ice added to the bath, the animal's temperature almost stopped falling and only continued to fall when the water was again made to circulate at the higher temperature. We have not found manual stirring of the water to be effective.

The patient's temperature is measured with a two-channel thermistor-type electric thermometer made by Light Laboratories. This is used for no purpose other than surgery under hypothermia, and is checked frequently against a standard mercury thermometer, whose accuracy has itself been checked by the National Physical Laboratory. It is felt that this is an important precaution, as we have found that electric thermometers, though necessary, can easily be made inaccurate by accidental damage.

Oesophageal and pharyngeal temperatures are

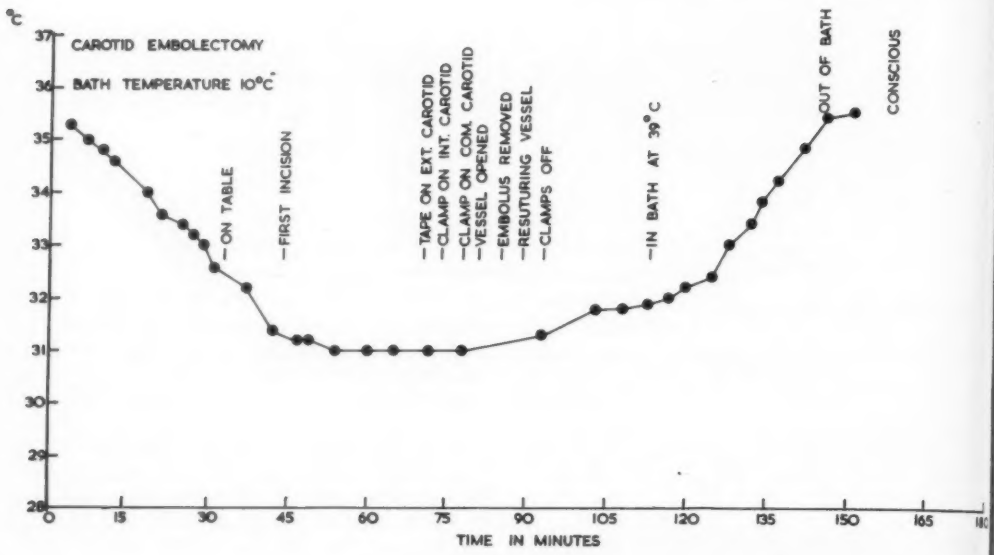

FIG. 3

Rate of cooling and rewarming produced by adequately stirred bath water. Patient of average build.

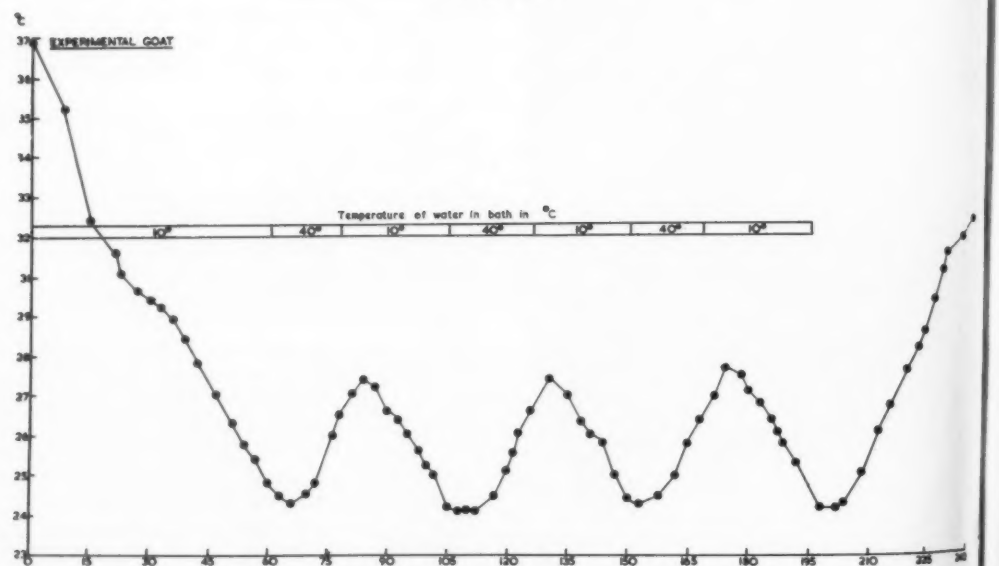

FIG. 4

Rate of change of temperature produced by moving water on hairy animal (goat).

measured and the pharyngeal temperature is taken to be an approximation to the cerebral temperature (Lucas, 1956).

The pharyngeal temperature may lag well behind the oesophageal temperature, particularly in a fat patient, so the circulation of the patient's blood is not stopped until the desired pharyngeal temperature has been reached (29–30°C). The oesophageal temperature is watched very carefully as an indication of the temperature of the heart. An assistant surgeon is asked to remain scrubbed and ready during the cooling process in case ventricular fibrillation should occur, although this has not happened with any of our cases.

blanket and we have been able to adjust the patient's temperature up or down with ease by this method. The fine control of temperature achieved by the water blanket is illustrated in figure 5. Water at 40°C is always circulated through the blanket some while before intracardiac manipulations, so that when the circulation is restored there is warm blood returning to the heart from the superficial tissues.

No. 16 hypodermic needles as electro-encephalographic electrodes are inserted into the patient's scalp as soon as he is on the operating table. No special orientation of these needles is necessary since the changes looked for are com-

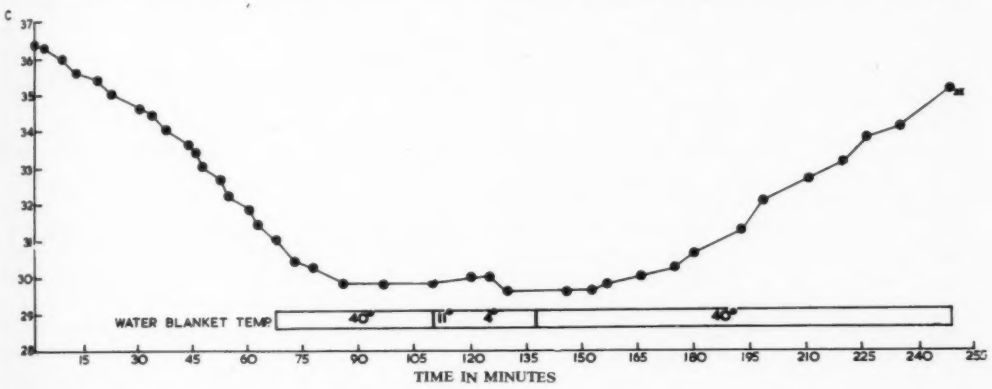

FIG. 5

Fine control of patient's temperature produced by water blanket after initial cooling in bath.

The patient is removed from the bath when his oesophageal temperature is such as to allow for the after-drop that always occurs. He is then dried with a towel and put on the operating table on which there is already a P.V.C. water blanket (Sellick, 1957), through which water at 40°C is circulating. This is pumped in and out of a sink adjacent to the operating theatre, by a small mains-operated pump, and the water is maintained at the desired temperature by a competent nurse armed with an accurate thermometer. The water blanket is wrapped round the patient's legs and lower abdomen. A single blanket only has been used for the more recent cases and has been found to be quite adequate. If the desired body temperature is not reached by the after-drop, cold or cool water is circulated through the water

paratively gross, and are distributed over the whole cortex. Parieto-occipital electrodes on one side have been found to be satisfactory and convenient. The electro-encephalographic electrodes are not inserted while the patient is in the bath, as the circulating water causes too much disturbance. No polarization troubles have ever been experienced during an extensive use of needles for electro-encephalography during anaesthesia. The electro-encephalogram and electrocardiogram are recorded on a two-channel electro-encephalographic apparatus. They are also monitored continuously on a two-channel Nagard oscilloscope. A technician is employed routinely as a record keeper during the procedure, as careful records are invaluable for the postoperative study of the cases. A physics technician is

also present to help with electrical apparatus.

The electro-encephalogram has been found to be of more use than the electrocardiogram; changes in the electrocardiogram are not necessarily reflected in changes of the circulation to vital organs, whereas the electro-encephalogram is a most sensitive indicator of cerebral hypoxia. For example, the placing of tapes loosely round the venae cavae, particularly the inferior vena cava, preparatory to cutting off the circulation, usually causes signs of some cerebral hypoxia (slow waves). When this occurs further cardiac manipulations are avoided until the electro-encephalogram returns to normal (fig. 6). When the circulation is completely stopped, anoxic signs, i.e. slow waves, and disappearance of the cortical output (fig. 7) appear, in a time varying from half a minute to as long as 2 minutes. Activity should begin to reappear within 10 minutes after restoration of the circulation. We believe that if the electro-encephalogram does not show some signs of cortical activity within this time the cause should be sought. For example, one patient with pulmonary stenosis died because although the valvular stenosis was relieved the associated infundibular stenosis was not sufficiently improved, and so the cardiac output was actually reduced by the operation (Brock, 1957). Recovery of activity as shown on the electro-encephalogram did not occur.

Neostigmine 0.03 mg per stone (6.3 kg) is injected into the aorta, close to the heart, after clamping, to reduce the risk of fibrillation (Prevedel et al., 1954; Sellick, 1955), and, although this arrhythmia has occurred but rarely, one should be ready for it at any time. We believe that defibrillation will only be possible if the causes of the fibrillation are removed. Without going deeply into the matter, which is a subject of much discussion well summarized by Gray (1958), it may be assumed that cardiac hypoxia and cardiac hypothermia play an important part. Therefore, should fibrillation occur, cardiac massage is started at once to improve the cardiac oxygenation as well as to preserve the vital centres. The chest is filled with saline at 40°C, to warm the heart muscle, and then electrical defibrillation is attempted.

To prevent increasing the cardiac hypothermia, should haemorrhage occur, a bottle of blood is put into the sink which has previously been filled with water at 40°C for the water blanket. This blood should not be kept warm for longer than

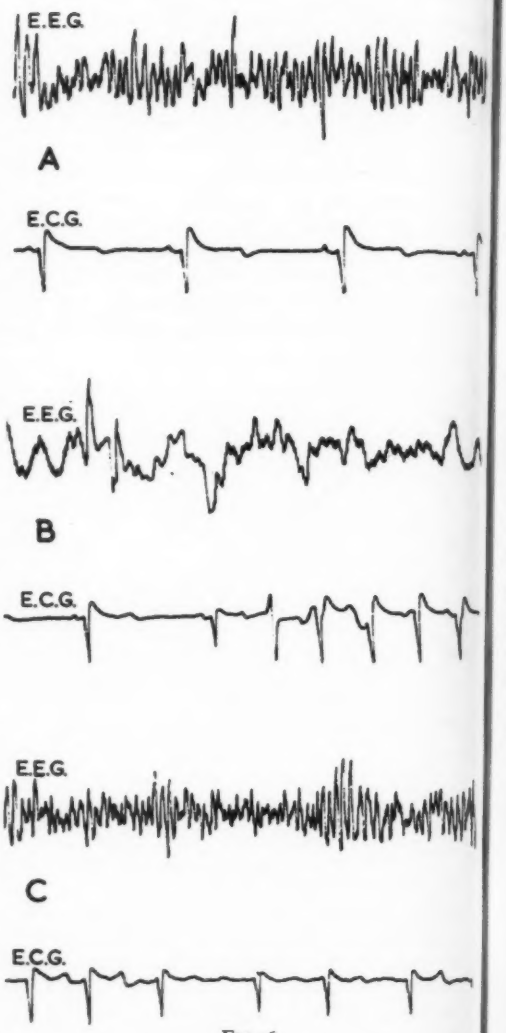

FIG. 6

Electroencephalogram of patient undergoing cardiac surgery. Showing effect of placing tapes loosely round the inferior vena cava.

(A) Before placing of tapes.
(B) Shortly after placing of tapes.
(C) A few minutes later showing recovery of alpha rhythm.

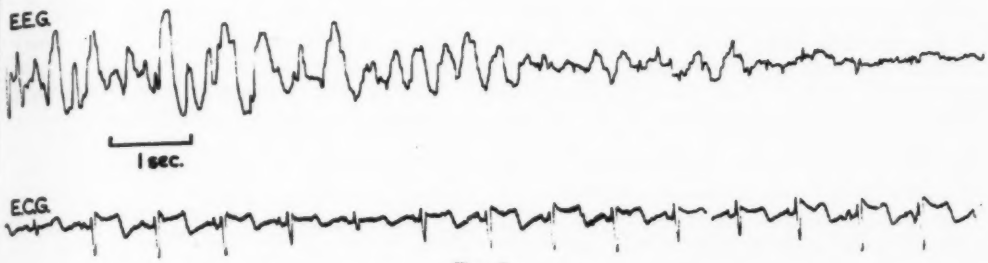

FIG. 7

Electroencephalogram showing slow wave response followed by suppression of cortical activity produced by compression of the venae cavae under hypothermia.

3 hours, but should be discarded if not used within this time for fear of rapid bacterial multiplication and the results of metabolic changes (high serum potassium, etc.). The danger of rapid transfusion of ice-cold blood was well illustrated in a case of abdominal aneurysm operated on under normothermic conditions. Sudden severe haemorrhage necessitated the rapid transfusion of 5 pints (2500 ml) of blood in about 5 minutes. The patient's heart stopped beating. Unfortunately monitoring equipment was not being used at the time so it is not known if the heart stopped in diastole or fibrillated. The surgeon was asked to do cardiac massage, and remarked that the heart was "ice cold". An oesophageal thermometer was passed soon afterwards and registered 31°C. This patient suffered no ill effects whatever from the accident, but one does not like to think what his temperature might have been had he been hypothermic before the transfusion. If one bottle of blood is kept warm others can be warmed quite quickly if it seems that they will be needed.

The electro-encephalograph, apart from its use for assessing the cerebral circulation after intracardiac manipulations, during cardiac massage, etc., has shown us that, after a period of hypoxia due to circulatory standstill, the brain is more sensitive to anaesthetic agents, and that deeper anaesthesia will occur without alteration in the concentration of the anaesthetic (fig. 8). It will be remembered that N_2O and O_2 usually causes flat-

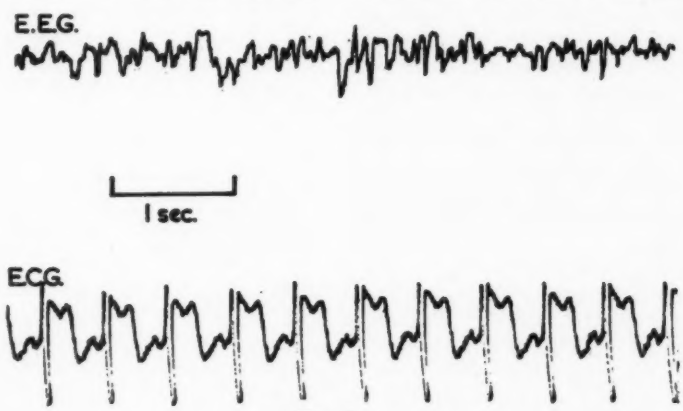

FIG. 8

Electroencephalogram from the same patient as fig. 1, 80 minutes after restoration of circulation, showing deeper anaesthesia and absence of alpha rhythm produced by higher concentration of O_2 with N_2O than before. There is no evidence of hypoxia.

tening and desynchronization of the alpha waves as the anaesthetic deepens. We feel, therefore, that this is further good reason for giving very light anaesthesia: and, if this is not employed, an absence of cortical output seen on the electro-encephalogram after restoration of the circulation may be merely a sign of deeper anaesthesia and not necessarily due to inadequate circulation.

It should be remembered that a desynchronized cortical output such as is found with moderately light N_2O and O_2 may be practically indistinguishable from "noise" arising from a fault in the apparatus. We had such a case where an apparently normal, desynchronized cortical output was coming from a loose valve in the first stage of the amplifier! Electrocardiographic interference may appear on the electro-encephalogram. This may be detected by the activity occurring synchronously with the heart-beat as shown on the electrocardiogram. With the moderate hypothermia that has been used the electrocardiogram has not been found to be as useful as might have been expected; for although well marked electrocardiographic changes have occurred, it has been difficult to estimate their significance in relation to the ultimate survival of the patient. However, an electrocardiograph should be employed if only to give immediate warning of ventricular fibrillation, or cardiac standstill. It is perhaps not out of place to stress here that if reliance is to be placed on elaborate and delicate apparatus, the user should understand and be able to service the equipment, even if, in fact, he employs someone else to do this.

In most of our cases the patient has been rewarmed sufficiently rapidly with the water blanket not to need immersion in warm water in the bath at the end of the operation, but this may be necessary if a patient is very fat, or the operation very short.

The anaesthesia is discontinued when the patient's temperature reaches 35°C. He should recover consciousness almost at once.

Atropine and neostigmine have rarely been necessary to reverse the paralysis produced by tubocurarine, and it has often been noticed under hypothermia that this drug appears to have less effect than usual. Confirmation that this is to be expected has recently been published (Zaimis, 1958).

SUMMARY

Some details of the technique of surface cooling are discussed. The anaesthesia used is very light, and no attempt is made to produce vasodilatation greater than that provided by N_2O and O_2 and tubocurarine. Drugs to produce vasodilatation are considered to be unnecessary, particularly as warmer water than usual is used to cool the patient. This has been found to produce rapid cooling if adequately stirred.

Electro-encephalographic changes associated with anaesthesia and cardiac manipulations are considered, and the apparatus is thought to be of great clinical value; the electrocardiogram, though necessary, has not been found to be as useful.

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INCOMPATIBLE BLOOD TRANSFUSIONS DURING OPERATION

BY

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RECOGNITION of haemolytic transfusion reactions in conscious patients is usually not difficult. Shortly after the onset of an incompatible blood transfusion, the conscious patient generally develops a variety of symptoms (Wiener, 1943), such as a sensation of fullness in the head, generalized tingling, precordial oppression and sudden sharp pain in the lumbar region. He becomes anxious, restless and dyspnoeic. His face is suffused and the neck veins are distended. Nausea and vomiting are not uncommon. These initial signs and symptoms may be followed by circulatory collapse, marked by hypotension, a rapid feeble pulse, and cold clammy skin; more rarely, pilo-erection and cyanosis appear. About an hour later, the patient commonly has a shaking chill and an elevation in temperature. Occasionally, chills and fever alone or in combination are the presenting signs of haemolytic reaction, the initial symptoms being unrecognized or absent. A haemorrhagic tendency can develop during or immediately after transfusion, and blood may ooze from the transfusion site, from the gums, uterus (in postpartum patients), or from any incised tissue. The appearance of this clinical complex makes recognition of haemolytic transfusion reactions in the conscious patient relatively simple.

The unconscious patient or one undergoing operation, however, is unable to manifest the initial group of symptoms (fullness in the head, precordial oppression, etc.), and the only signs indicating that a haemolytic reaction has been taking place are those which tend to develop as the reaction becomes more advanced, i.e., sudden hypotension and/or oozing. During operation, diagnosis becomes still more difficult and uncertain, because even when present, hypotension and oozing are easily attributed to events incident to anaesthesia, operation, or both. Thus haemolytic transfusion reactions occurring during operation are generally not recognized early and their ambiguous clinical manifestations are too often treated with additional incompatible blood. For example, a recent analysis of incompatible transfusions (Binder, Ginsberg and Harmel, 1959) showed that those patients who underwent operation received the larger volumes of incompatible blood and sustained the majority of fatal reactions. These findings indicate that earlier recognition and treatment of haemolytic transfusion reactions during operation is of utmost importance. The following case reports are therefore presented to detail the subtle manner with which haemolytic reactions appear during operation in the hope that this experience will lead to earlier recognition and more effective treatment.

Ten patients were given incompatible blood during operation. The case reports are summarized in table I and presented below. In addition, one patient is discussed who had been successfully treated for a severe haemolytic transfusion reaction and then subjected to emergency operation.

Since hypotension is by far the most common and frequently the only sign of a haemolytic reaction, the cases are presented according to the following classification:

(A) No hypotension.
(B) Hypotension.
  (1) Preceding and continuing after the incompatible transfusion.
  (2) Appearing only after the incompatible transfusion.

CASE REPORTS

(A) No Hypotension.

Case I.

A girl of 11 years was admitted because of a congenitally dislocated hip for reconstruction of the acetabulum. The history was otherwise of no consequence and the pertinent physical findings were limited to the hip. The blood pressure was 110/70 mm Hg; pulse rate 72/minute; haemoglobin 14 grams per cent; urine normal. The blood group was reported as AB positive.

Pre-anaesthetic medication: pethidine 25 mg and atropine 0.4 mg, was given 1 hour before operation. In the operating room, the blood pressure was 100/40 mm Hg, the pulse rate 126/minute.

Anaesthesia was induced with thiopentone 75 mg and maintained with cyclopropane using a closed circuit and assisted respiration. In anticipation of excessive blood loss, a transfusion of blood was begun early in the operation. The blood loss was an estimated 400 ml; the blood pressure and pulse rate remained constant during the 1½-hour procedure.

The immediate postoperative course was uneventful. The patient regained consciousness rapidly and experienced neither hypotension nor tachycardia afterwards. The next day the temperature was normal, but the abdomen was slightly distended and the patient vomited several times. As she had not urinated, the bladder was catheterized and 450 ml of grossly blood-stained fluid was obtained. The haemolytic reaction was confirmed when the blood was regrouped and shown to be A positive, not AB positive.

In spite of the smooth operative and early postoperative course, the patient became oliguric. Diuresis occurred after 4 days of renal shutdown and the patient recovered.

Case II.

A man aged 71 was to have a partial cystectomy for carcinoma of the urinary bladder. Pertinent physical findings included: signs consistent with a moderate, obstructive emphysema; e.c.g. indicating an uncomplicated sinus tachycardia; blood pressure 145/85 mm Hg; haemoglobin 14 grams per cent; and one-plus haematuria. The blood group was reported to be A positive.

Pre-operative medication: pethidine 35 mg and atropine 0.4 mg, was given 1½ hours before operation, but the patient appeared apprehensive and the effect of the drugs was considered unsatisfactory. Eleven mg of an amethocaine-dextrose solution with 0.1 mg of adrenaline was prepared (a total volume of 2.4 ml) and injected intrathecally. The initial sensory level was at T10; 15 minutes later it had ascended to T6.

Apparently because the patient was restless and garrulous, the spinal analgesia was supplemented with intravenous pethidine and in the next 2 hours 100 mg were given intermittently. During this interval the blood pressure gradually fell from 160/80 to 120/80 mm Hg, but the pulse rate remained at 76 to 80 per minute and the patient appeared in no distress.

In spite of minimal blood loss, a transfusion with A positive blood was begun. Ten minutes later the patient began to complain of epigastric pain. Because the anaesthetic level was believed to be inadequate, general anaesthesia was induced with cyclopropane. The patient was then intubated, and surgical anaesthesia was maintained with a light ether-oxygen mixture employing a semiclosed circuit.

Twenty minutes later, immediately following closure of the peritoneum and removal of skin drapes, an increased ooze was seen issuing from the cut surfaces. Attempts to secure haemostasis were unsuccessful. Nevertheless the wound was closed, but bleeding became so profuse that 1,000 ml of citrated blood, cross-matched from the patient's original specimen, was pumped in rapidly under pressure. A haemolytic reaction apparently was not suspected until 2 hours after the haemorrhagic diathesis had been recognized; for only at this time was a specimen of venous blood finally taken for study. It was grossly haemolyzed and did not clot.

The persistent bleeding was treated with 5 grams of fibrinogen, after which the wound was reopened and packed. The blood was also regrouped, and when it was found to be B positive and not A positive, a litre of correctly grouped blood was administered. One and a half hours after therapy had been directed to the clotting effect, i.e., 4 hours after the haemorrhagic diathesis was first noted, the bleeding had essentially stopped. The patient who had been anaesthetized during this entire period, was finally allowed to awaken.

Although the blood pressure and pulse rate had remained at his normal level throughout this episode, he became completely aneuric. In addition, his postoperative course was complicated by a progressively severe intractible ileus. The patient died with ileus and renal failure on the fifth postoperative day. An autopsy was not granted.

Case III.

A man of 65 was admitted for exploratory laparotomy. He had a history marked by anorexia, pain, nausea, and weight loss, consistent with acute cholecystitis overlying chronic hepatocellular disease. Pertinent findings on physical examination included: temperature 102.6°F; pulse rate 62/minute; respiration 24/minute; blood pressure 114/66 mm Hg; right upper quadrant tenderness; pedal oedema; and râles at both lung bases. Laboratory examination revealed haemoglobin 13 grams per cent; two-plus albuminuria; liver investigations indicated both hepatic and obstructive disease; and an e.c.g. revealed an intraventricular conduction defect and evidence of myocardial damage. An intravenous cholangiogram was read as "no visualization". The blood group was reported as B positive.

The anaesthetic course is illustrated in figure 1. Pethidine 100 mg, and atropine 0.4 mg, given 1 hour before operation, produced adequate sedation. Continuous spinal anaesthesia was attempted using an intrathecal catheter. The catheter was placed without difficulty, and 16 mg of an amethocaine-dextrose solution (4 mg/ml) was injected in divided doses. Although a satisfactory sensory level was not obtained, the patient noted that his extremities had become warm. In addition, the pulse rate fell from 64 to 50 per minute.

As the anaesthetic drug was believed to be defective, 5 per cent procaine-dextrose was prepared, and 125 mg of this solution was introduced through the catheter. Again no sensory level was obtained, and after a half-hour wait, general anaesthesia was induced with 325 mg of thiopentone. The trachea was intu-

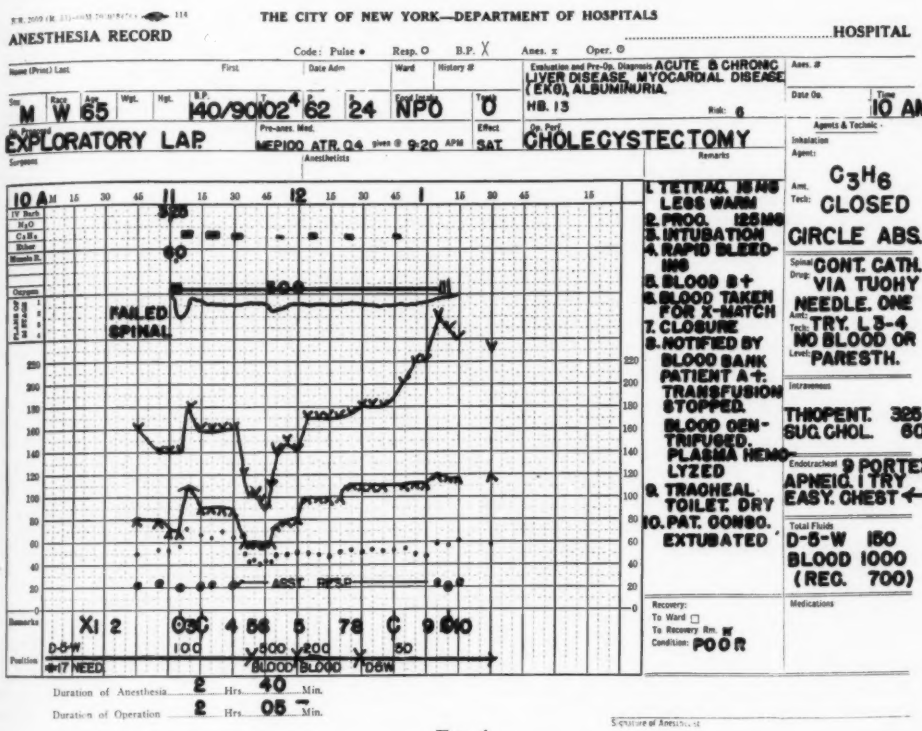
THE CITY OF NEW YORK—DEPARTMENT OF HOSPITALS
ANESTHESIA RECORD
HOSPITAL
Code: Pulse • Resp. O B.P. X Anes. x Oper. ⊙
M W 65
140/90 102 62 24
NPO
0
HB. 13
ACUTE & CHRONIC LIVER DISEASE, MYOCARDIAL DISEASE (EKG), ALBUMINURIA.
EXPLORATORY LAP.
MEPIOO ATR. 0.4
CHOLECYSTECTOMY
10 AM
C3H6
CLOSED
CIRCLE ABS.
CONT. CATH. VIA TUOHY NEEDLE. ONE TRY. L 3-4 NO BLOOD OR PARESTH.
THIOPENT. 325
SUC. CHOL. 60
9 PORTEX APNEIC. I TRY EASY. CHEST
D-5-W 150
BLOOD 1000
(REC. 700)
1. TETRAG. 15 MG LEGS WARM
2. PROC. 125 MG
3. INTUBATION
4. RAPID BLEEDING
5. BLOOD B+
6. BLOOD TAKEN FOR X-MATCH
7. CLOSURE
8. NOTIFIED BY BLOOD BANK PATIENT A+: TRANSFUSION STOPPED. BLOOD CENTRIFUGED. PLASMA HEMOLYZED
9. TRACHEAL TOILET. DRY
10. PAT. CONSC. EXTUBATED
FAILED SPINAL
ASST. RESP.
Recovery: To Ward ☐ To Recovery Rm. ☒ Condition: POOR
Duration of Anesthesia 2 Hrs. 40 Min.
Duration of Operation 2 Hrs. 05 Min.

FIG. 1

Anaesthetic record of patient described as case no. III. The illustration shows the hypertension which followed an incompatible blood transfusion.

bated with a no. 10 cuffed tube, and surgical anaesthesia was maintained with intermittent cyclopropane in a closed circuit. The gall bladder, densely adherent to liver, stomach, omentum and abdominal wall, made dissection very difficult, and bleeding was brisk. The blood pressure soon fell from 160/100 to 100/60 mm Hg, and the first of two transfusions with B positive blood was begun. Incidentally, a sample of venous blood was withdrawn in order to cross-match additional blood. After 700 ml of incompatible blood had been transfused, the blood bank reported that this second sample was A positive, not B positive.

The patient's blood pressure had not fallen with the incompatible transfusion. Instead, it was returned to its pre-operative level (140/80 mm Hg) with the first bottle of blood, the pulse rate remaining at 40 to 50 per minute. With the beginning of the second transfusion less than a half-hour later, the patient became hypertensive. At first the blood pressure was elevated to 170/100 mm Hg, but at the close of the procedure 1 hour later, it had ascended to 240/120 mm Hg. The pulse rate still remained at 50 to 60 per minute. The marked hypertension (230/120 to 180/100 mm Hg) lasted for 7 hours, then gradually decreased during the next 9 hours to its usual range, 140/90 mm Hg. Nevertheless, the 24-hour urine output was 300 ml. The oliguria persisted for 4 days. His course thereafter was relatively uncomplicated and he was discharged a month later.

Discussion.

The absence of hypotension makes the diagnosis of haemolytic transfusion reaction inordinately difficult. In a certain number of reactions, cardiocirculatory and bleeding disturbances may be completely lacking; and in common with "silent" transfusion reactions in conscious patients, the first inkling of their occurrence is the appearance of oliguria several days later. Case I typifies the silent reaction. Infrequently, a haemorrhagic diathesis may be the only significant sign, hypotension being completely absent. This is illustrated in case II. Also of interest in

this case was the development of epigastric pain shortly after the incompatible transfusion was begun. In retrospect, this symptom may have signalled the onset of the haemolytic reaction, but unfortunately, it was thought to be the result of an ineffective level of spinal analgesia. Therefore, inhalation anaesthesia was undertaken which effectively masked other possible symptoms, and incompatible blood was transfused until the coagulation defect became obvious. It is conceivable that had the transfusion been discontinued when epigastric pain appeared, the haemorrhagic diathesis would not have occurred.

Although sudden hypotension is the most common cardiocirculatory disturbance associated with haemolytic reactions, other aberrations in haemodynamics such as tachycardia and hypertension also occur. The difficulty has been that hypertension and tachycardia are often attributed to other causes. Indeed, the cause of the persistent hypertension in case III was not investigated. That it could have been related to a haemolytic reaction was not even considered, and only after the diagnosis had been made by accident was this relationship finally entertained.

(B) *Hypotension.*

(1) Hypotension preceding Incompatible Transfusion

Case IV.

An obese female aged 40 years was admitted for hysterectomy with a diagnosis of fibroid uterus. The history and physical examination were otherwise noncontributory. The blood pressure was 150/70 mm Hg; pulse rate 64/minute; haemoglobin 9 grams per cent; urine normal. The blood group was reported as B positive.

The pre-anaesthetic medication, atropine 0.4 mg and pethidine 100 mg, was clinically satisfactory. A lumbar puncture was performed with ease and 16 mg of amethocaine in 1.6 mg of 10 per cent dextrose-water and 0.4 mg of adrenaline (total volume 2 ml) was injected intrathecally (fig. 2). Immediately preceding lumbar puncture, an injection of 20 mg of methamphetamine was given intramuscularly. The initial sensory level was said to be at T6; the height of the sensory level was not further recorded. That it may have crept somewhat higher is suggested by the fact that the patient's blood pressure fell to 90/50 mm Hg, the pulse rate remaining at 64 per minute. A phenylephrine infusion (0.01 mg/ml) was begun and 1 mg was administered within 10 minutes. The blood pressure responded promptly, but because it fell again when administration of the vasopressor was halted, the infusion was continued for the major part of the procedure.

Fifteen minutes before the end of the operation the phenylephrine was again stopped. The blood pressure promptly fell to 60/40 mm Hg. Although an estimated 300 ml of blood had been lost, 500 ml of blood was transfused rapidly, but without effect on the blood pressure. The phenylephrine infusion was then restarted, and the blood pressure again was returned to the pre-operative level of 130/70 mm Hg.

The poor response to transfusion suggested the possibility of transfusion reaction. The bladder was then catheterized, but as the urine was macroscopically clear, a second transfusion was begun. When 100 ml had been administered the patient began to have shaking chills. The blood was discontinued and the vasopressor again restarted. At this time, venous blood was finally withdrawn for study. On centrifugation unmistakable haemolysis was revealed and the haemolytic transfusion reaction was confirmed when, on regrouping, the patient's blood was O positive and not B positive as originally determined.

The operation having ended, the patient was sent to the ward. There, O positive blood was pumped in rapidly under pressure and noradrenaline substituted for the phenlyephrine infusion. After 2,500 ml of blood had been administered, the blood pressure was 110/70 mm Hg, haemoglobin 11.5 grams per cent. Approximately 4½ hours after the first transfusions of incompatible blood had been begun, the patient suddenly and unexpectedly gasped and died. At that moment blood appeared at the mouth and rectum.

At necropsy, bleeding was demonstrated from all mucous and serous membranes. In addition, between 1 and 2 litres of unclotted blood was found in the abdominal cavity. The ligatures were secure.

Case V.

A man of 72 years was brought to surgery for suprapubic prostatectomy. Except for the present disease, phsyical findings and past history were noncontributory. The blood pressure on admission was 150/80 mm Hg; pulse rate 62/minute; haemoglobin 11.5 grams per cent; e.c.g. indicated sinus bradycardia. The blood group was reported as AB positive.

Pre-anaesthetic medication, pentobarbitone 100 mg and atropine 0.4 mg, was given 1½ hours before operation. The blood pressure immediately before induction of anaesthesia was 120/80 mm Hg, the pulse rate 68 per minute. Spinal analgesia was initiated with 10 mg of amethocaine-dextrose solution. The initial sensory level was at T10; no later evaluations of the level were recorded. Twenty minutes later, the blood pressure fell to 100/80 mm Hg and the pulse rate to 56 per minute. When divided doses of intravenous methamphetamine failed to produce the desired response, 500 ml of AB positive blood was transfused rapidly. The blood pressure rose to 140/80 mm Hg where it remained for the next half-hour. The pulse rate also gradually climbed to 80 per minute.

Forty-five minutes after the start of the transfusion, the blood pressure suddenly fell to 80/60 mm Hg. At this time, excessive bleeding was noted issuing from the suprapubic catheter. Although the blood loss was thought to be small, the blood pressure could no longer be measured and the patient had become cold, clammy and disoriented. A second bottle of AB positive blood was transfused rapidly. The wound was reopened and a generalized ooze observed. Since no bleeding point could be found, the fossa was packed and the wound reclosed.

A transfusion reaction was then suspected. Venous blood was obtained which showed haemolysis and inability to clot. The blood was immediately re-

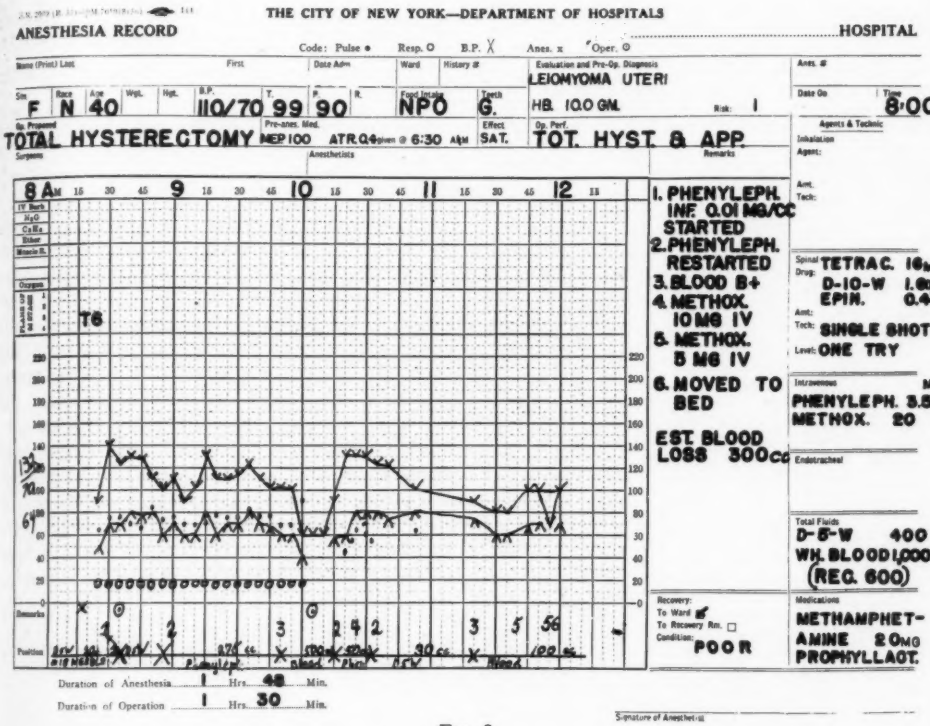

FIG. 2

Anaesthetic record of patient described as case no. IV. The illustration shows the poor response of the blood pressure to transfusion with incompatible blood and the difficulty in distinguishing between the hypotension produced by the spinal anaesthetic and that associated with transfusion reaction.

grouped and found to be O positive, not AB positive. Massive transfusion with O positive blood was begun, and in the following 2½ hours, 8,500 ml of blood, 750 ml of fibrinogen, and 1,000 ml of fresh-frozen plasma were administered without effect. Finally, in a vain attempt to secure better haemostasis the wound was reopened, but the bleeding could not be controlled and the procedure was abandoned.

The patient was returned to the ward. His blood pressure was 90/60 mm Hg, pulse rate 100 to 120 per minute. An infusion of phenlyephrine was started. He continued to bleed and to receive citrated blood. Twelve hours after transfusion of the first bottle of incompatible blood, he had received a total of 17,500 ml of blood plus additional fibrinogen and fresh-frozen plasma; but the coagulation defect pesisted. Only then was the patient returned to the operating room for direct transfusions. After 500 ml had been transfused, the patient died. Consent for necropsy was not obtained.

Case VI.

A man aged 36 was admitted to the hospital after having been struck by an automobile and sustaining a compound fracture of the left leg. Following admission, he became progressively drowsy and finally lost consciousness. A paraplegia developed on the left side and he lapsed deeper into coma. The patient was then brought to surgery for emergency craniotomy. The blood pressure was 130/80 mm Hg; pulse rate 60/minute; respirations, hyperpnoeic at 16/minute; haemoglobin 14.5 grams per cent; urine negative. The blood group was mistakenly reported as B positive.

No pre-operative medication was given. The scalp was infiltrated with 1 per cent procaine, and the craniotomy was performed. Both subdural and epidural haemorrhages were found; in addition, the brain was contused and lacerated. Although the operative blood loss was small, the patient's blood pressure fell to 100/70 mm Hg and the pulse rate increased to 120 or 130 per minute. Presuming these events to be signs of hidden haemorrhage at his leg fracture site, a transfusion of B positive blood was begun. Twenty-five minutes later, the pulse rate suddenly increased to 180 per minute. The blood pressure rose concomitantly from 110/70 to 140/90 mm Hg; but unlike the

pulse rate which remained elevated, it gradually fell in the next 45 minutes to 100/80 mm Hg. This minimal hypotension and persistent tachycardia prompted a second transfusion of incompatible blood. However, this transfusion did not affect his pulse rate and blood pressure.

The craniotomy was completed in 2½ hours, and the patient was returned to the ward in critical condition. There he continued to receive incompatible blood until 6 hours after his return, when a fresh venous sample taken to cross-match additional blood was regrouped and shown to be A positive, not B positive.

In spite of vigorous treatment of the then recognized haemolytic reaction, the patient's condition deteriorated steadily. During the first 24 hours he excreted only 200 ml of muddy urine. The coma deepened and generalized spasticity became more and more prominent. A second craniotomy was undertaken to decompress the brain, but when the flap was reopened, the patient developed rapid Cheyne-Stokes respiration. The blood pressure fell precipitously to 70/40 mm Hg and the pulse rate increased to 140 per minute. The brain bulged out of the wound under marked pressure and the procedure was finally abandoned. No epidural or subdural bleeding was seen and haemostasis was normal. The patient continued to worsen and died 4 days later.

At necropsy, the positive findings were limited to the head and leg fracture.

Case VII.

An 18-year-old primigravida was admitted in the 36th week of gestation in active labour. Admission history and physical examination revealed: a blood pressure of 116/80 mm Hg; pulse rate 65/minute; haemoglobin 10 grams per cent, but the haematocrit taken 1 day later was 41 per cent and the plasma fraction was slightly icteric. X-ray pelvimetry revealed a borderline contracted pelvis. The blood group was reported as AB positive.

Labour was protracted and ineffective, and when hypotonic uterine dysfunction developed, the patient was scheduled for caesarean section under spinal anaesthesia. As only one bottle of AB positive blood was available, a unit of low titre O positive blood was also cross-matched.

Unfortunately, the anaesthetic record is inadequate. The pre-anaesthetic medication, if any, was not stated. Spinal analgesia was attempted with a hyperbaric amethocaine solution, but the amount of agent used and the anaesthetic level achieved were not recorded. However, inasmuch as the spinal analgesia was supplemented with nitrous oxide-ether, it was probably unsatisfactory. Both bottles of blood (O positive and AB positive) were used. The order and time of their administration was not recorded; nor was the indication for transfusion given.

Toward the end of the procedure, the blood pressure became imperceptible and the pulse rose to 170 per minute. The operation was completed rapidly and the patient returned to the ward still hypotensive. There, a noradrenaline infusion was started which elevated the blood pressure to 80/? mm Hg. The haematocrit at this time was 32 per cent and the plasma fraction was deep yellow. On catheterization of the bladder, no urine was obtained.

Because of hypotension and icterus, liver failure was diagnosed. A transfusion reaction was not considered until 13 hours later, when 30 ml of mahogany-coloured urine finally was obtained. The patient's blood was then regrouped and shown to be B positive, not AB positive as originally reported.

In spite of supportive therapy including increasing doses of noradrenaline and transfusion with compatible blood, the patient died 44 hours after operation. At necropsy, the findings were consistent with both acute haemoglobinuric nephrosis and extensive liver necrosis.

Discussion.

Hypotension preceded incompatible blood transfusion in four patients. In two, hypotension was precipitated by high levels of spinal analgesia attempted in hypovolaemic patients; in the remainder, the patient's precarious surgical status rather than the anaesthetic management seemed to be the predisposing cause. In each instance, the blood transfusion (of incompatible blood) did not restore cardiocirculatory stability. This finding, although not invariable, may be of diagnostic significance when it does occur. Unfortunately, except when other manifestations of haemolysis (chills, increased bleeding) were also present, the correlation between haemolytic transfusion reaction and continuing or deepening hypotension was not made.

(2) Hypotension appearing only after Incompatible Transfusion

Case VIII.

A woman aged 40 was to have a radical vulvectomy and bilateral groin dissection for carcinoma of the vulva. Apart from pruritus, burning during micturition, and vulvar leukoplakia, the admission history and physical examination were not significant. The blood pressure was 120/70 mm Hg; pulse 80/minute; haemoglobin 14.5 grams per cent; and two-plus albuminuria. The blood group was erroneously reported as A positive.

The pre-anaesthetic medication, morphine 10 mg and atropine 0.4 mg, produced a satisfactory clinical effect. Anaesthesia was induced with cyclopropane-oxygen, the trachea intubated without difficulty, and surgical anaesthesia maintained with cyclopropane and "top ether" using a closed circuit (fig. 3). In anticipation of excessive blood loss, the first of three incompatible blood transfusions with A positive blood was begun. For 3 hours, the pulse rate remained stable at 90 per minute and the blood pressure at 140/80 mm Hg; but 25 minutes after the start of the third transfusion, the pulse rate gradually rose to 120–140 per minute and the blood pressure became unrecordable. Ten minutes later the blood pressure was 100/60 mm Hg by palpation. The gravimetrically estimated blood loss was 1,000 ml.

The operation having been completed, the patient was returned to the ward still unconscious. There, she remained unconscious for 6 hours, much longer than could be accounted for by the anaesthetic. In addition, the blood pressure fell again from 90/60 mm Hg to 50/?. The bladder was catheterized but

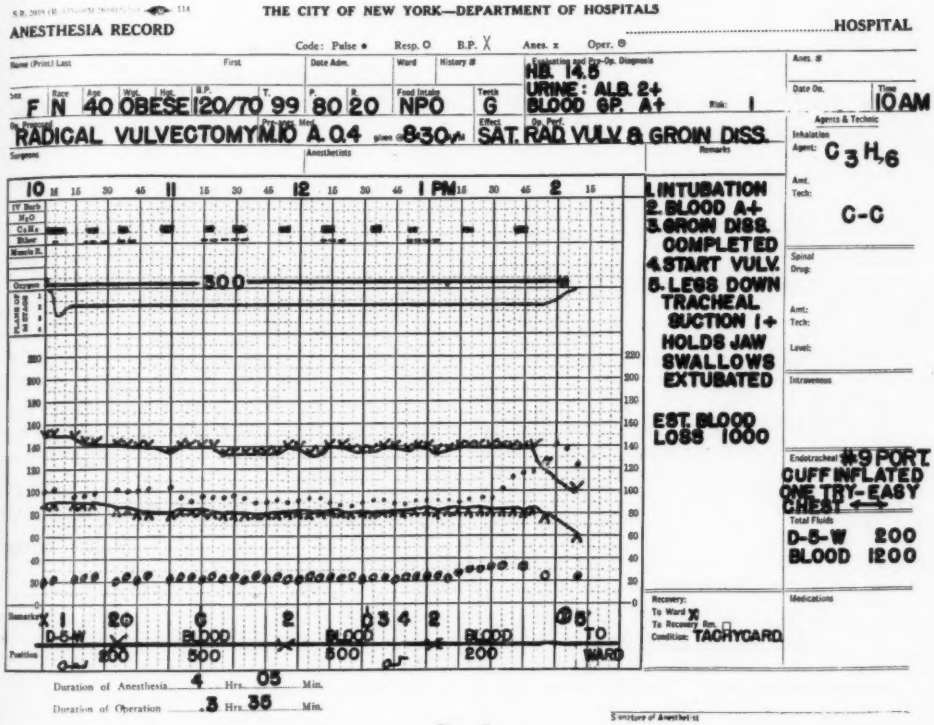

FIG. 3

Anaesthetic record of patient described as case no. VIII, The illustration suggests that hypotension and tachycardia may appear some time after the onset of incompatible blood transfusions.

no urine was obtained. At this time the blood bank requested to regroup a second sample of the patient's blood because the original recipient tubes were thought to have been interchanged. Regrouping showed the blood to be O positive and not A positive. A haematocrit (41 per cent) revealed haemolysis.

The hypotension was treated with a noradrenaline infusion. When it was discontinued 5 hours later, the blood pressure remained stable at 130–140/70–90 mm Hg. After this hypotensive period the patient was oliguric (380 ml/24 hours) for 36 hours. The oliguria is difficult to assess for it is not an unusual finding following radical pelvic operations. The only indication that kidney function may have been affected by the haemolytic transfusion reaction was that two consecutive Fishburg concentration tests taken 3 weeks later showed her unable to concentrate urine.

Case IX.

A 36-year-old hypertensive multipara was brought to the operating room 4 hours after delivery for emergency hysterectomy because of postpartum uterine atony. She had had eclampsia and pre-eclampsia with earlier pregnancies. On this admission the blood pressure was 182/150 mm Hg and the urine examination revealed one-plus albumin; but neither had changed significantly during pregnancy and the patient was not believed to have toxaemia. The history and physical examination otherwise revealed nothing. The haemoglobin was 9.5 grams per cent. The blood group was reported to be A positive.

In spite of oxytocics, she had bled intermittently in the interval between delivery and operation and had received 3,000 ml of blood. The blood pressure had remained stable, but the pulse rate gradually increased to 120 per minute. Since an opiate or barbiturate was thought to be ill-advised under these conditions, the pre-anaesthetic medication consisted solely of atropine 0.4 mg.

The anaesthetic course is shown in figure 4. Induction and maintenance of anaesthesia was with cyclopropane in a closed circuit. The blood loss continued to be profuse, and during the 1½ hour operation, the patient was transfused with an additional 5,000 ml of blood pumped in under pressure. When the peritoneum was closed, a generalized ooze was seen. As citrate intoxication was suspected, calcium gluconate was given intravenously which apparently controlled the

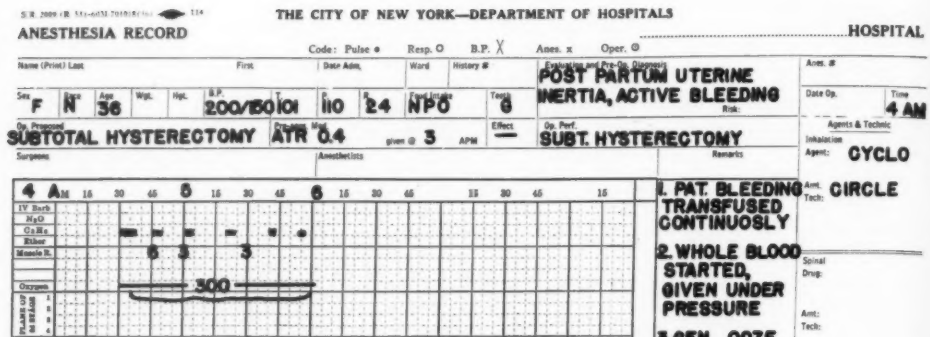

FIG. 4

Anaesthetic record of patient described as case no. IX. The illustration shows the difficulty in differentiating between the generalized ooze of citrate intoxication and that associated with haemolytic transfusion reaction.

bleeding. Inspection of the blood bottles, however, revealed one to have contained A positive and not O positive blood.

The patient's blood pressure remained at 170/114 mm Hg and the pulse rate at 130 per minute until she arrived at the ward. There, she became hypotensive, necessitating the use of noradrenaline and additional transfusions of 1,000 ml of blood. After 3 hours the blood pressure became stable at her normal hypertensive level.

The subsequent postoperative course was very stormy, complicated by acute renal failure of 8 days duration, severe postpartum psychosis, convulsions, and a wound dehiscence. She was finally discharged 7 weeks after admission.

Case X.

A woman of 31 was admitted to the hospital with a 6-weeks history of threatened abortion. One hour prior to admission, she began to bleed profusely and claimed to have aborted. Physical examination was noncontributory. Haemoglobin was 13 grams per cent; urine normal. The blood group was O positive. The patient continued to bleed briskly and was brought to surgery for emergency curettage.

Pre-anaesthetic medication, pethidine 75 mg and atropine 0.4 mg, was given intramuscularly 15 minutes before operation. Its effect was satisfactory. The blood pressure immediately before operation was 110/80 mm Hg, pulse 96 per minute.

On induction of anaesthesia with cyclopropane, the pulse and blood pressure became unobtainable. The anaesthetic was immediately discontinued, the uterus rapidly evacuated of large amounts of clot and tissue, and a transfusion begun. The pulse and blood pressure quickly returned to normal. The patient regained consciousness and was returned to the ward in good condition.

Two hours later, the patient had received only 100 ml of blood. Suddenly she had a rigor. The bladder was catheterized and "dark amber" urine obtained. A haematocrit likewise revealed haemolysis. Rechecking her blood against that remaining in the bottle showed that the bottle had been mislabelled, and that the patient had been given A positive not O positive blood.

The blood pressure, 130/110 mm Hg immediately after transfusion and then 140/90 mm Hg, gradually fell during the next hour to hypotensive levels. Treatment with noradrenaline and correctly grouped blood, however, soon restored normal blood pressure. The urine output remained normal and the patient was discharged 2 days later.

Discussion.

Hypotension following an incompatible transfusion is generally not an immediate finding. In contrast to the early subjective responses, it tends to appear 1 or 2 hours later, when it is more likely to be attributed to postanaesthetic hypotension or continued bleeding than to incompatible transfusion. An interesting manifestation of haemolytic reactions is a change in the patient's behaviour. This may present as drowsiness, lethargy, anxiety, and other aberrations in the state of consciousness or awareness. In case X, the patient remained unconscious postoperatively considerably longer than could be accounted for by the anaesthetic.

Case XI.

A primigravida of 43 years was brought to surgery for emergency hysterectomy. She had been admitted at term in active labour. The admission history and physical examination were noncontributory. The initial blood pressure was 140/80 mm Hg; pulse 80/minute; temperature 101.8°F. The blood group was reported as A positive.

She subsequently underwent an uneventful Caesarean section for amnionitis. Postoperatively, because of sepsis and an estimated 750 ml blood loss, a transfusion was begun. After 300 ml of A positive blood had been transfused, the patient was found sweating and irrational. The blood pressure was unobtainable. The uterus was flaccid and an estimated 1,500 ml of liquid blood was seen in the bed. Uterine atony was diagnosed. Thereupon, the remaining 200 ml of blood was pumped in under pressure followed by another bottle of A positive blood. At the same time, a new specimen was sent to be cross-matched against additional blood. This sample showed the patient to be O positive, not A positive. Meanwhile, the patient had received 1,000 ml of incompatible blood.

Energetic transfusion with O positive blood, fibrinogen and fresh-frozen plasma was begun. With transfusion, the blood pressure climbed to 90/60 mm Hg, but a tachycardia of 160 per minute persisted and the patient continued to bleed profusely from the nose, mouth, vagina and incision. Fourteen hours later, after she had received 15,000 ml of O positive whole blood, 22 grams of fibrinogen and 700 ml of fresh-frozen plasma, the bleeding apparently stopped. The coagulation mechanism seemed to be restored, as evidenced by a normal clotting time with good clot retraction and stability. The blood pressure at this time was 100/60 mm Hg, the pulse 140 per minute. The total urine output was 225 ml of bloody urine.

Four hours later, although the clotting mechanism remained good, bleeding per vagina started anew. The uterus was again flaccid and unresponsive, and the blood pressure was 70/40 mm Hg. A noradrenaline infusion was begun. In view of the uterine atony, an immediate subtotal hysterectomy was undertaken. Atropine 0.4 mg was given intravenously 5 minutes before operation.

Induction of anaesthesia was with thiopentone (125 mg), and endotracheal intubation was performed with the aid of 80 mg of suxamethonium. Anaesthesia was maintained with nitrous oxide-oxygen in a semiclosed circuit. Nine mg of d-tubocurarine was given at the time of incision.

When 2,000 ml of blood and clots were found in the abdominal cavity, the patient was transfused with an additional 1,500 ml of whole blood and, prophylactically, with 3 grams of fibrinogen. The blood pressure remained at 100/60 mm Hg throughout the 40-minute procedure, but the pulse rate was elevated from 90 per minute to 140 per minute. Haemostasis was adequate and the patient was returned to the ward, conscious but in critical condition.

Postoperatively, the patient's status continued to worsen. The blood pressure fell again. Noradrenaline effected only a transient and ineffectual response and the patient died 7½ hours later.

At necropsy, examination revealed several litres of blood and clots in the abdomen, lower nephron nephrosis, partial pulmonary atelectasis, and agonal liver necrosis.

Discussion.

The case is presented to illustrate the difficulties in management of a patient subjected to operation after surviving a severe haemolytic reaction and prolonged haemorrhage. The clotting defect apparently manifested itself as uterine bleeding, but a haemolytic reaction was not suspected. The "uterine atony" was therefore treated with oxytocics and still more incompatible blood until the correct diagnosis was finally made by the blood bank.

EVALUATIONS AND CONCLUSIONS

Eleven case reports are presented in which haemolytic transfusion reactions are associated with operation. Six patients died, five recovered. Three deaths (case nos. IV, V, XI) were a direct result of incompatible blood transfusions. In each instance, the immediate cause of death was intractible, generalized, exsanguinating haemorrhage. The patients' ailment probably was the primary factor in the remaining three deaths (case nos. II, VI, VII); however, renal failure secondary to incompatible blood transfusion undoubtedly contributed to their eventual demise. Of the five patients who survived, four (case nos. I, III, VIII, IX) developed an oliguria which lasted from 36 hours to 8 days. The fifth (case no. X) received only 100 ml of incompatible blood before the transfusion reaction was discovered,

Case no.	Age	Sex	Blood group		Operation	Anaesthetic	Reason for transfusion	Volume incompatible blood transfused (ml)	Initial signs and symptoms	How diagnosis was made	Initial treatment	Outcome
			Patient	Donor								
I	11	F	A+	AB+	Reconstruction of acetabulum	Ether	Anticipated blood loss	500	None	Haematuria	None	Oliguria 4 days; recovered
II	71	M	B+	A+	Partial cystectomy	Spinal + ether	Gradual fall in blood pressure	1500	Epigastric pain; increased ooze	Haemolyzed plasma	Fibrinogen	Oliguria 5 days; ilius; died 5th day
III	65	M	A+	B+	Cholecystectomy	Cyclopropane; failed spinal	Operative blood loss with hypotension	700	Hypertension	Notified by blood bank	None	Oliguria 4 days; recovered
IV	40	F	O+	B+	Hysterectomy	Spinal	Hypotension from anaesthetic	600	Rigor; continuing hypotension	Haemolyzed plasma	Noradrenaline	Hidden bleeding; died 4½ hours
V	72	M	O+	AB+	Prostatectomy	Spinal	Hypotension from anaesthetic	1000	Generalized ooze; continuing hypotension	Haemolyzed plasma	Blood, fibrinogen, fresh-frozen plasma	Intractible bleeding; died 13 hours
VI	36	M	A+	B+	Craniotomy	Local	Tachycardia hypotension	2500	Tachycardia; continuing hypotension	Notified by blood bank	Blood, fibrinogen, fresh-frozen plasma	Increasing coma and spacticity; oliguria; died 4 days
VII	18	F	B+	AB+	Caesarean section	Spinal + N_2O-ether	Unknown	500	Hypotension; tachycardia	Haematuria	Noradrenaline	Oliguria; increased jaundice; died 44 hours
VIII	40	F	O+	A+	Radical vulvectomy groin dissection	Cyclopropane	Anticipated blood loss	1500	Hypotension; tachycardia; prolonged unconsciousness	Notified by blood bank	Noradrenaline	Oliguria 36 hours; recovered
IX	36	F	O+	A+	Hysterectomy	Cyclopropane	Operative blood loss	500	Generalized ooze	Incorrect bottle discovered	Noradrenaline; blood	Oliguria 8 days; recovered
X	31	F	O+	A+	Curettage	Cyclopropane	No blood pressure on induction	100	Rigors; haematuria	Haemolyzed plasma	Noradrenaline; blood	No oliguria recovered

and this patient had no evidence of kidney dysfunction. Significantly, all but this patient received 500 ml of blood or more, and all but this patient had severe and, in several instances, fatal transfusion reactions. This finding supports the contention that the severity of incompatible blood transfusion reactions tends to increase with the volume of blood transfused.

Thus, to avoid excessive transfusion with incompatible blood, early diagnosis of transfusion reactions is of paramount importance. However, in this series of cases, it was not possible for either of the two cardinal signs of haemolytic transfusion reaction in the operated patient, intractable oozing or hypotension, to warn the surgeon or anaesthetist as to the possibility of transfusion reaction. Indeed, only two reactions (case nos. IV, X) were recognized early.

A haemorrhagic diathesis developed in four patients. In cases II and IX the increased bleeding was the only sign of incompatible transfusion, while in cases XI and V, bleeding and hypotension appeared together.

The significance of intractable oozing when present alone was not appreciated. In case II, the bleeding was assumed to be routine and consequently was treated with two more bottles of incompatible blood. In case IX, citrate intoxication was considered to be the cause of the coagulation defect and the incompatible transfusion was continued after intravenous calcium gluconate had been given. Only after inspection of the bottles of previously administered blood revealed one to have contained incompatible blood was the haemolytic reaction recognized and the blood taken down.

Not even when increased bleeding and hypotension appeared together was the diagnosis made. In case XI the haemorrhage was thought to be due to uterine atony (in retrospect, the reverse may have been true); while in case V a discrete bleeding point was first postulated to explain the haemorrhage. Only after much time had been spent in a fruitless search for a hypothetical bleeding point did the combination of bleeding and hypotension suggest the correct diagnosis.

This study indicates that the aetiology of a haemorrhagic diathesis secondary to transfusion reaction is not readily appreciated. Other causes often invoked are: citrate intoxication, vitamin K deficiency, congenital clotting defects, hypothermia, liver disease or usual surgical blood loss. Unfortunately, incompatible blood is usually continued while these causes are either treated empirically or ruled out.

Hypotension, too, may be ascribed to a great variety of causes. A partial list includes: preexisting hypotension, chronic hypovolaemia, surgical blood loss, congestive failure and myocardial infarction, pre-anaesthetic medication, deep general anaesthesia, and a too-high level of spinal analgesia. Some of the problems of recognition of incompatible transfusion reactions in the face of hypotension are illustrated in these case presentations. It is significant that of the six patients in whom hypotension was observed relatively early, the only one in which the reaction was soon recognized was the patient in whom low blood pressure appeared in conjunction with a rigor (case no. IV).

An analysis of the record clearly shows that the responsible physician is often not sufficiently aware of the possibility of a haemolytic transfusion reaction. This is particularly distressing, because once it is considered, the diagnosis is extremely simple. When a transfusion reaction is suspected, the following course is suggested. The transfusion should be stopped at once. If volume replacement becomes necessary, a plasma-volume expander may be used. Dextran may not be the preferable expander because of its possible relation to late coagulation defects (Langdell, et al., 1958). An oxalated venous specimen is centrifuged for 3 to 5 minutes which is sufficient to reveal haemolysis. Urine haemoglobin determinations are not performed at this time as early urine samples are not readily obtainable or sufficiently reliable (see case nos. IV, VII).

If haemolysis is demonstrated or if a haemorrhagic diathesis is suspected, intensive study of the possible coagulation defect is instituted. However, since time is of the greatest importance, a sample of blood is immediately regrouped and cross-matched with fresh blood which was collected by gravity drainage into plastic containers. Transfusion of fresh blood should be begun without delay.

The use of fresh blood for all bleeding problems is suggested, because the deficient clotting

factor or factors are not predictable; nor can one afford the time to await their determination. Instead, while these tests are conducted, the patient is given the only substance which is known to have adequate quantities of all clotting factors, namely, fresh blood collected in the manner described or by direct transfusion. When the deficient factor(s) is identified, it is administered, when possible, to reinforce the effect of fresh blood.

However, even though recognition is prompt and treatment optimum, one must remember that in the natural course of a haemolytic reaction, hypotension and possibly bleeding are relatively late manifestations One or two hours have often elapsed from the beginning of transfusion before these signs have appeared and one can begin to suspect its presence. During this interval, the incompatible transfusion is often continued and the severity of the reaction thereby increased.

Since the clinical circumstances peculiar to the anaesthetized surgical patient present such serious obstacles to the early recognition of haemolytic transfusion reactions, the indications for blood transfusion during operation must be carefully assessed. Attention should be directed toward restoration of blood volume pre-operatively whenever feasible. The need for relatively small amounts of blood (500 ml or less) during operation should be especially considered, and deferred whenever possible until the patient regains consciousness.

SUMMARY

Eleven case reports are presented which illustrate the circumstances surrounding the administration of incompatible blood and the development of incompatible transfusion reactions during anaesthesia. Unlike the clinical picture manifested by conscious patients, the signs of transfusion reaction in this group of patients were generally limited to hypotension, generalized oozing, or both; and incompatible transfusion reactions which develop during operation may be classified on this basis. Because the coagulation defect may be unrecognized, and because both hypotension and increased bleeding are commonly attributed to other causes, the incompatible transfusion reaction is not suspected until late and the patient therefore treated with still more incompatible blood.

The coagulation defects associated with incompatible transfusion reactions are not clearly defined. The authors suggest that fresh whole blood is the only substance which provides all clotting factors, and should therefore be the initial therapy of any acute coagulation defect.

Since diagnosis and treatment of incompatible transfusion reaction are uniquely difficult during operation and in the immediate postoperative period, the authors stress that the greater hope for decreasing the incidence of incompatible transfusion reactions in the surgical patient lies in more adequate preparation of the patient with regard to pre-operative blood volume replacement and more judicious use of blood during operation.

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Brit. J. Anaesth. (1959), **31**, 229

A STRAIN GAUGE FOR PHYSIOLOGICAL USE

A Preliminary Communication

BY

G. E. HESSE

Department of Anaesthetics, University of Bristol

THIS strain gauge has been developed for investigation into respiratory movements, particularly in neonates. It consists of a fine rubber tube filled with aqueous colloidal graphite. The dimensions of the rubber tube used are: bore $1\frac{1}{2}$ mm, wall thickness $\frac{3}{4}$ mm, and length 24 cm. The resistance of this assembly is 300,000 ohms. The electrodes consist of silver tubes, 2.4 mm ($\frac{3}{32}$ inch) bore, 0.4 mm (1/64 inch) wall thickness and length 1.2 cm ($\frac{1}{2}$ inch), to which the rubber tubes are tightly tied. Electrical connection is provided by a small pin silver-soldered to the silver tube (fig. 1). Short lengths of rubber tube are fitted over the open ends of the electrodes prior to filling with colloidal graphite and sealed afterwards by clamping with small pieces of lead sheet. One should ensure that the gauge is well sealed and it is inadvisable to use silicone rubber owing to its permeability.

The strain gauge is used in a bridge network (fig. 2) with a voltage source of between 1.4 volts and 9 volts, depending on the sensitivity required.

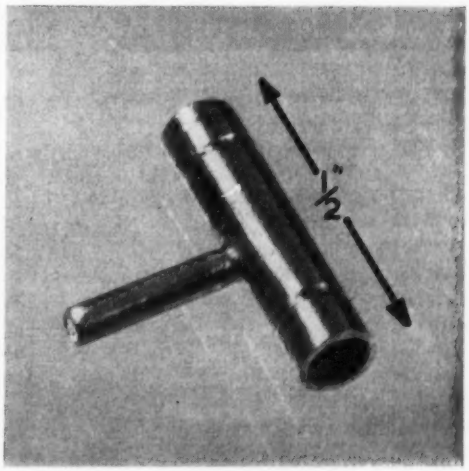

FIG. 1

Electrode.

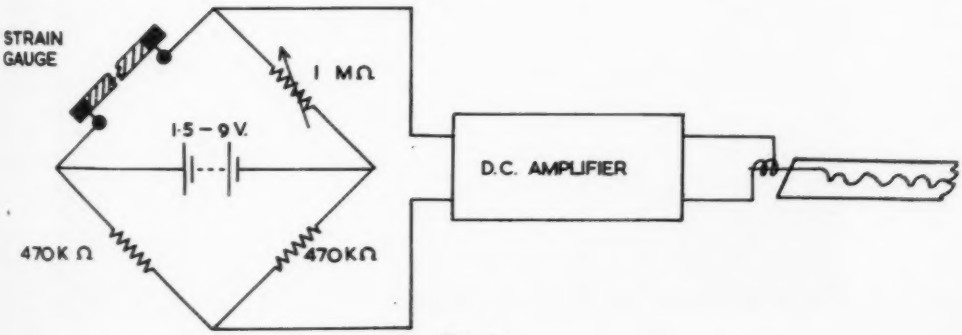

FIG. 2

Circuit diagram showing strain gauge coupled into bridge network, etc.

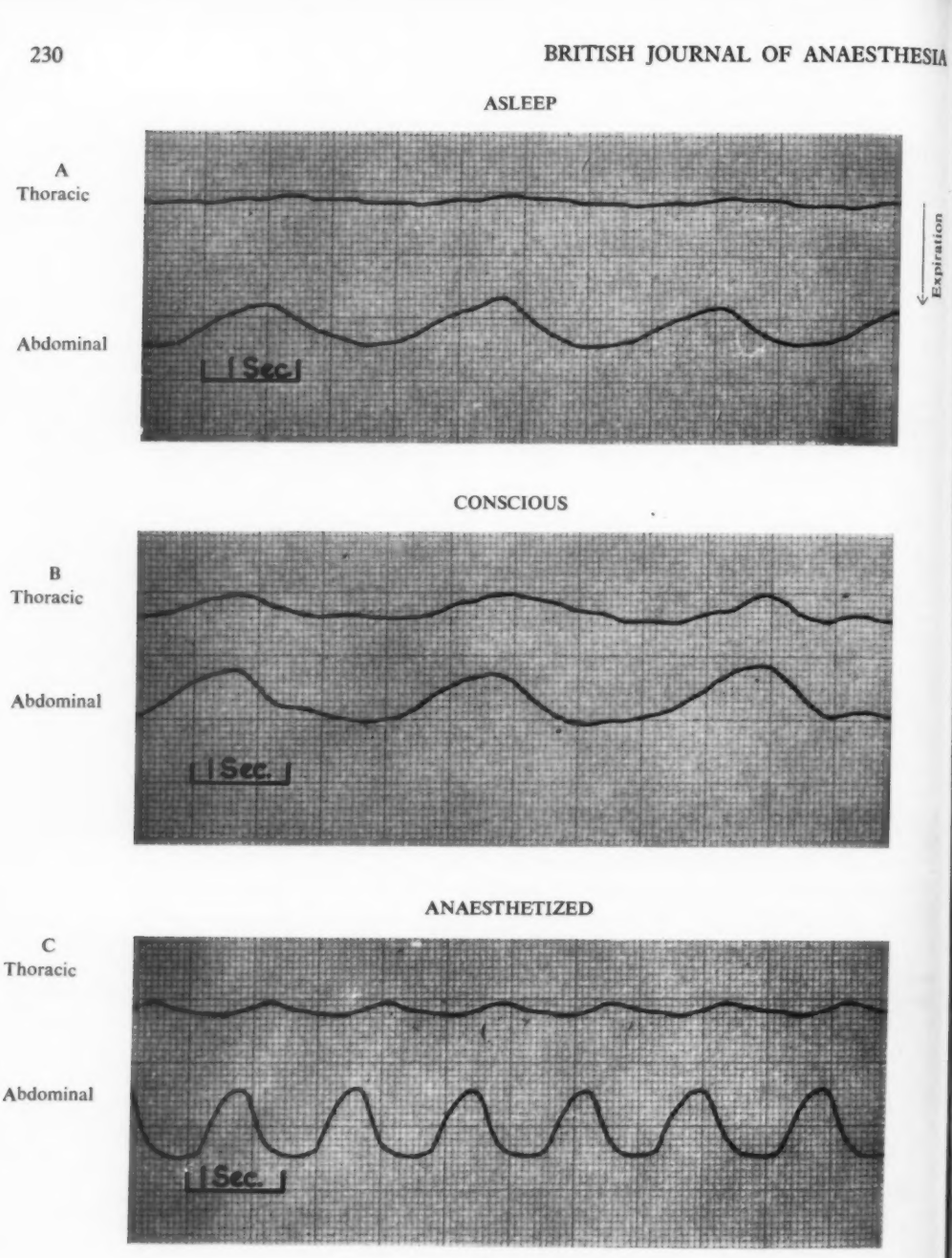

FIG. 3
Recordings taken of a 6-year-old boy supine.

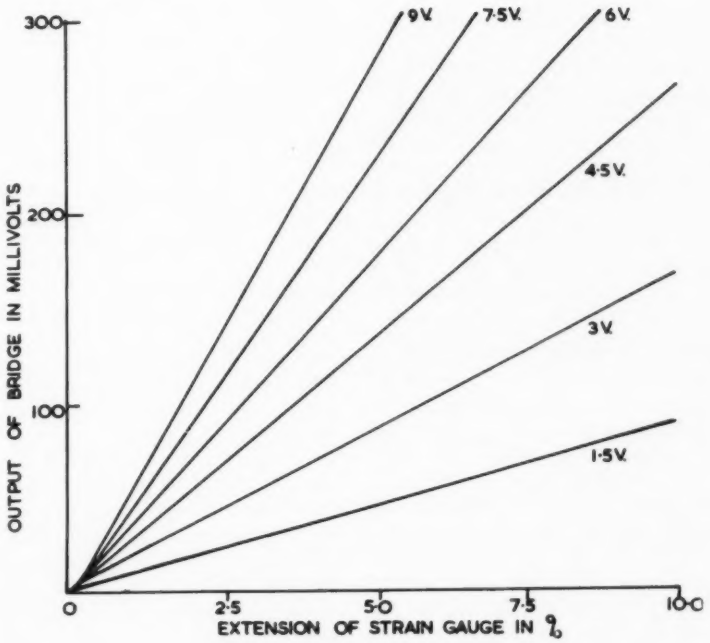

FIG. 4

Sensitivity of strain gauge when used with circuit illustrated in fig. 2 showing output for various voltages.

The output is taken to a standard D.C. amplifier and writer.

The strain gauge increases in its resistance by 2 per cent for every 1 per cent increase in extension, and the relationship between resistance and extension is linear. The graph shown (fig. 4) relates the voltage output of the bridge to the extension of the strain gauge for different values of battery. There is no detectable noise although there is a slight steady voltage of a few millivolts at the electrodes due to polarization. No drift from this cause has been encountered.

To illustrate the use of the apparatus recordings are shown (fig. 3) of thoracic and abdominal movements during respiration of a supine subject whilst (A) asleep, (B) conscious and (C) anaesthetized. The way that the thoracic movement lags behind the abdominal during anaesthesia is well shown.

Samples of aqueous colloidal graphite were kindly supplied by Acheson Colloids Ltd., Prince Rock, Plymouth, under the trade name of "Aquadag".

Brit. J. Anaesth. (1959), **31**, 232

FROM THE MORBIDITY CONFERENCE

A CASE OF MYOCARDIAL INFARCT UNDER ANAESTHESIA

BY

J. ROBINSON

Royal Southern Hospital, Liverpool

A WOMAN aged 35 was presented for a plastic repair of the right renal pelvis. Both kidneys had been shown on i.v.p. to be hydronephrotic, with impaired function, more severe on the right side.

Pre-operative examination revealed an apprehensive, thin woman of 8 stone 5 lb (53 kg), with a blood pressure of 210/130 mm Hg. Examination of the fundi revealed no abnormality, nor was any cardiac enlargement noted clinically or on radiography of the chest. Her exercise tolerance was excellent. The haemoglobin was 105 per cent and the blood urea 36 per cent.

Seven days previously retrograde pyelography had been carried out without difficulty, using thiopentone 150 mg, nitrous oxide, oxygen and trichloroethylene as anaesthesia.

On this occasion premedication with morphine 10 mg and atropine 0.6 mg was given 1 hour before induction. After the usual test dose a total of 25 mg. of d-tubocurarine was given, followed by 125 mg of thiopentone. The lungs were inflated with a 50/50 mixture of nitrous oxide and oxygen for 3 minutes and a tube passed. Anaesthesia was maintained with a 2-to-1 nitrous oxide/oxygen mixture, administered via a circle type absorber, a further 5 mg of tubocurarine being required to maintain control of respiration. The blood pressure at this stage was 200/120 mm Hg.

The operation was begun through a right anterior transverse approach. Bleeding was not severe, but the loss was replaced as it occurred with a slow blood transfusion. During mobilization of the kidney the blood pressure fell suddenly to 100/90 mm Hg and there was a severe bradycardia of 36 beats per minute. Atropine 1.2 mg was given intravenously and the pulse rate rose to 90 per minute and the blood pressure to 180/90 mm Hg. Within 10 minutes the systolic pressure had fallen to 90 mm Hg and the diastolic could not be determined, although the pulse rate remained unchanged. At this point 1 pint (500 ml) of blood had been transfused. Methoxamine 10 mg was given intravenously without effect, nor was there any response to a further 5 mg.

A noradrenaline drip 1/250,000 gave an initial response, the blood pressure rising to 110/70 mm Hg and the pulse to 120 per minute. However, within 5 minutes the blood pressure fell to 40 mm Hg systolic, accompanied by a tachycardia of 180 beats per minute. The latter was an expected response to noradrenaline after atropine administration, but this together with the lack of vasopressor effect led to the abandonment of the noradrenaline drip.

Acute adrenocortical insufficiency was postulated and hydrocortisone 50 mg was given intravenously, and as there was a slight rise in the blood pressure this was followed by a further 50 mg without effect.

By now the patient showed evidence of fairly extensive vasoconstriction with marked "goose flesh". The peripheral pulses were now absent; only a slow (36 beats per minute) carotid pulse could be felt; the pupils had begun to dilate.

A quick reappraisal of the situation suggested that the hypotension must be cardiac in origin, because (*a*) blood loss had been adequately replaced, (*b*) there had been no real response to vasopressors and (*c*) no response to the blood drip. Therefore a 1/250,000 adrenaline infusion was set up. The pulse returned to the wrist with a rate of 140 per minute and a systolic pressure of 60 mm Hg, and these effects could be maintained by the drip.

With the completion of the operation the curarization was reversed by giving neostigmine 1.25 mg intravenously slowly and without atropine. However, as the pulse rate dropped gradually to 70 per minute from 160 per minute, atropine 0.6 mg was given, followed by a further 1.25 mg of neostigmine. Good reversal was obtained.

Coincident with the onset of spontaneous respiration and awakening, pulmonary oedema occurred and about 1 pint (500 ml) of blood-stained, frothy fluid was removed by endobronchial suction. Controlled respiration with oxygen alone effectively cleared up the pulmonary oedema. The acute left ventricular failure was treated with strophanthin 0.5 mg given intravenously. Other methods of lowering the venous pressure, such as the administration of hexamethonium, were considered but discarded, and aminophylline was thought to be unlikely to be better than strophanthin.

The adrenaline drip was stopped when the blood pressure was stable at 80/40 mm Hg with a pulse rate of 90 per minute; 1 mg of mersalyl was given intravenously to promote a diuresis. An e.c.g. taken at this time showed no abnormality other than sinus tachycardia and low voltage. On clinical grounds alone a left ventricular myocardial infarct was suspected.

Any movement by the patient precipitated attacks of pulmonary oedema which could be controlled by positive pressure respiration and endobronchial suction. To ensure quiescence after such an attack, a 50/50 N_2O/O_2 mixture was administered via the endobronchial tube for 10–15 minutes.

The attacks of pulmonary oedema became less frequent and 19 hours after induction of anaesthesia the patient was extubated, the patient being alert and co-operative.

Convalescence from then on was uneventful, urinary output being excellent and serum chemistry remaining unchanged. The electrocardiogram the next day showed deep negative T-waves in all leads and 1 week later the negative T-waves in V6 had a slight S.T. depression, which 7 days later (i.e. 2 weeks after operation) had become more marked.

The diagnosis of a large left ventricular myocardial infarct occurring under anaesthesia was made.

CORRESPONDENCE

HYPOTHERMIA FOR COARCTATION?

Sir,—On page 95 of the March 1959 issue of your Journal I read "Hypothermia seems likely to remain the method of choice for patients requiring operation for coarctation of the aorta", whereas on page 125 of the same issue I read "Hypothermia is unnecessary in the correction of coarctation of the aorta in view of the extensive collateral circulation". Am I correct in continuing to assume the latter to be the generally accepted view?

W. N. ROLLASON

Physiology of Spinal Anaesthesia. By Nicholas M. Greene, B.S., M.D., M.A. Published by Baillière, Tindall and Cox, Ltd., London. Pp. 195. Price 48*s*.

The most interesting and important question in connection with the physiology of spinal anaesthesia is how an intrathecal injection of an anaesthetic can cause the death of a patient. This has been the subject of controversy for half a century; even so late as 1930 Koster said, "Very little is known about the various mechanisms by means of which death is produced". Professor Greene has his own view on this question; thus on page 24 he says: "Respiratory arrest and cardiovascular collapse do occur with high spinal anaesthesia. In some instances they are due to the paralysis of medullary nerve centres. But such paralysis is not attributable to the direct action of the spinal drug on the brain stem. The paralysis is instead a result of inadequate medullary blood flow secondary to extreme arterial hypotension." The life and functioning of the medulla like any other tissue in the body depends upon an adequate supply of oxygenated blood. If for any reason, such as severe arterial hypotension or haemorrhage, this is not forthcoming there will be failure, that is paralysis in this case. So far we shall all agree with the professor, but when he says, "But such paralysis is not attributable to the direct action of the spinal drug on the brain stem", he differs from CoTui (1932) who believed from his experiments in the early thirties, to which Professor Greene refers, that the paralysis was due just to that, namely the direct action of the drug on the respiratory and vasomotor centres. Work done in Manchester (Hill and Macdonald, 1933) in the early thirties, independent of and in ignorance of CoTui's work, supports the idea that the spinal drug acts directly on the respiratory centre causing paralysis, and this in the presence of a high blood pressure, a pressure which falls only when the heart fails as the direct consequence of the respiratory paralysis. Professor Greene's objection to CoTui's experiments, namely that he took no precaution to prevent the anaesthetic from travelling down the theca to affect the phrenics and intercostals, does not apply to the Manchester work as the dose used was 10 mg in 0.1 ml saline. Moreover it is there shown that phrenic paralysis is quite different in pattern from that due to a central paralysis and therefore there is no possibility of confusing the two.

The difference between these two views is not merely of academic interest for, if the professor is right, the Trendelenburg position will always be adequate to rescue the patient; but not only experimental work on cats but clinical experience shows that on occasion artificial respiration is essential to save the patient. This fact—for we are strongly of opinion that it is a fact—does not in the least diminish Professor Greene's oft-repeated insistence on the importance of the Trendelenburg position. It is obvious that in ordinary clinical medicine, when the injection is made in the lumbar region, the vasoconstrictors, the intercostals and the phrenics will all be affected before the respiratory centre, and suitable rescue measures will have already been put into action, including both the Trendelenburg position and artificial respiration. Amongst these suitable measures is the prophylactic use of a heavy solution rather than a light one. An excessive dose of a heavy solution will tend to spend itself on posterior roots to the comfort of the patient rather than on the anterior roots to his danger. If Professor Greene mentions this point I missed it.

The first two chapters of the book, in which these matters are discussed, are the most important and interesting and they occupy more than half of it. Professor Greene thinks spinal anaesthesia the choice in cases of phaeochromocytomas and that it has many advantages in obstetrics but must be in the hands of an anaesthetist familiar with the technique. There is an inde

and a very extensive bibliography. It is a good-looking book, a pleasure to possess, gives sound advice, and can be recommended with confidence.

E. Falkner Hill

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The Recovery Room. A symposium. Edited by John Adriani and John B. Parmley. Published by Charles C. Thomas, Illinois, U.S.A. Pp. 123; illustrated. Price 32*s.* 6*d.*

Presumably the purpose of presenting a book in the form of questions and answers is to enable the reader to gain the maximum amount of information with the minimum expenditure of time and effort. If this is what the forty-five authorities responsible for *The Recovery Room* intended, they have not been successful. Much concentration is required to read anything with so little literary appeal. One has to proceed by fits and starts through a series of disjointed statements some of which are so obvious that they offend.

It is a waste of valuable space to print the questions in full, because the answers are what the reader wants to know. Where there is agreement on these, this is only made clear by the rather artless device of repetition and where there is a divergence of opinion, there is little attempt to analyze the causes.

In the chapter entitled "Administration", the authors make an attempt at exact delineation of responsibility in the recovery room. This is both unnecessary and dangerous. In major surgery, to be successful, responsibility must be shared throughout the team in the recovery room as in the theatre itself. A tacit understanding to leave some frontiers of authority ill defined will lead to much better co-operation than an attempt at rigid definition. Any anaesthetist with aspirations in regard to control of the recovery room might pause to consider himself faced unaided with an emergency such as a slipped ligature from the pulmonary artery.

The recovery room bed on rollers which is well described should be adopted in this country. In the long list of other equipment considered necessary, the items are certainly not in order of importance. Those required for endotracheal intubation and oxygenation, likely to be the first steps in most postoperative emergencies, find only an insignificant place in the middle.

It is interesting to note the unanimous conclusion that the recovery room leads to no reduction in numbers of nursing personnel or in costs to the hospital, the sole reason for its existence being increased safety and efficiency. Such facts as these may be gleaned from perusal of this book.

Elizabeth S. N. Fenton

Acta de l'Institut d'Anesthesiologie, Volume VII, 1958. Published by Librairie Arnette, Paris, under the direction of Professor P. Moulouguet and T. Baumann. Pp. 268; 43 illustrations. Price 2500 francs.

This volume is as interesting as its predecessors and that is saying much. The emphasis of the various articles is on the clinical side and should therefore appeal particularly to the anaesthetist actually engaged in the day-to-day practice of anaesthetics. Such up-to-date matters as encephalography, halothane and tranquillizers are dealt with. Under the heading Classification of Tranquillizers we have "Aucune des classifications proposées n'est satisfaisante". So a drug is a tranquillizer or it isn't; drugs used for the purpose of tranquillizing fall into no other category. An extremely useful account is given of half a dozen of the most used. In the article on halothane reference is made to the report of the Medical Research Council which attributes the hypotension usually associated with induction of anaesthesia by halothane to cardiac depression. This view has now been abandoned by the authors of that report. Changes in the e.e.g. precede other clinical signs of cerebral hypoxia, falls of blood pressure, and cardiac inefficiency, and so are of great value. Not only in its present usefulness but also as a help in solving problems ahead of us the author expects the e.e.g. to make a considerable contribution.

The first article ends with the sentence "Dans tous les cas, qu'il s'agisse de 'bonnes paroles' ou de bonne drogues, on peut dire que la façon de donner vaux mieux que ce qu'un donne". Had it been the first sentence it could well have been the keynote of the whole chapter, a chapter that deals with the attitude of the doctor to his patient; a subject of the highest importance usually woefully neglected in our medical schools, where young men are taught to be clever, but they are not taught "Que le façon de donner vaux mieux que ce qu'on donne".

Transfusion and oxygenation are referred to as the time-honoured methods of treating cardio-vascular collapse, but I missed any notice of the drug (2831R.P.) chlorhydrate d'heptaminol which was so favourably reported on in Volume V of this series. Perhaps, like so many other drugs, it has failed to come up to its early promise. The upset of fluid balance is presented as being responsible for some of the strange happenings recorded in the chapter on "Accidents Nerveux Postoperatoires".

M. Legrain describes the tests of kidney efficiency it is desirable to make before any operation is undertaken. He divides patients into three categories according to the results of the various tests and warns against operation except as a last resource in category three. A favourable view is taken by Dr. Richet of the value of the artificial kidney.

The volume concludes with two short articles: one on explosions and the other on the sterilization of intratracheal tubes. These are immediately preceded by an account of the difficulties encountered in the introduction of these tubes in cases when the mouth is closed and cannot be opened. The causes of this condition, ankylosis of the temporo-maxillary joint, burns and subsequent scarring, destruction by accident or disease and finally severe infection as in Ludwig's angina are dealt with in turn and suggestions made to deal with them. Altogether a valuable and up-to-date account helpful to all practising anaesthetists.

E. Falkner Hill

Les Médicaments du Système Nerveux Cérébro-spinal. Published under the direction of Professor F. Mercier by Masson et Cie, Editeurs, Paris. Price 5800 francs.

This is a volume of 574 pages, 25 figures, numerous tables and chemical formulae. The French have the habit of spending their money on the contents rather than on the binding of their books, a custom which has our wholehearted approval. This volume, though paper backed, is a weighty one in the physical sense, but much more by reason of the weight of knowledge evident in its contents. There are twelve chapters, each dealing with a group of drugs having similar actions and uses. Thus we have anaesthetics general and local; relaxants acting at the neuromuscular junction; the latest inhalational anaesthetic, halothane; Artane and other drugs used for Parkinson's disease; morphia, atropine, the barbiturates—all are considered.

We hope at a future date to give a more detailed criticism, when we have been able to give the time which such a collection deserves.

E. Falkner Hill

Printed in Great Britain by JOHN SHERRATT & SON, Park Road, Altrincham

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